EXHIBIT 1

Statement of Uncontested Facts

REDACTED PUBLIC VERSION

I. NATURE OF THE DISPUTE

1. Plaintiffs Ingenus Pharmaceuticals LLC ("Ingenus") and Leiutis Pharmaceuticals LLP ("Leiutis") (together, "Plaintiffs") have sued defendant Accord Healthcare, Inc. ("Accord" or "Defendant") for infringement of U.S. Patent No. 10,993,952 under the patent laws of the United States, including 35 U.S.C. § 1 et seq.

2. Defendant does not challenge personal jurisdiction for this matter.

3. This Court has subject matter jurisdiction over this matter.

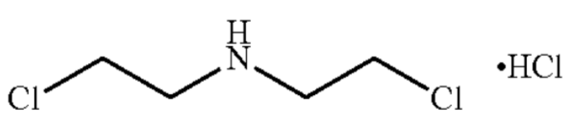
4. Defendant does not challenge venue for this matter.

II. THE '952 PATENT

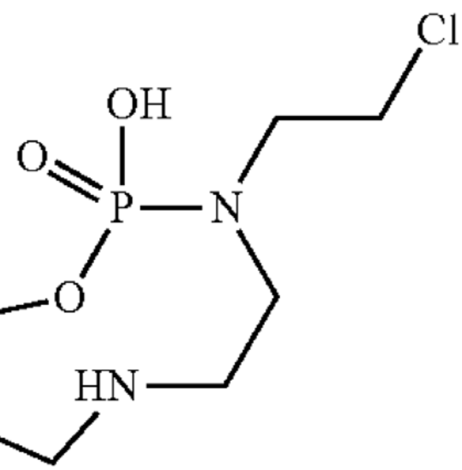
5. US. Patent No. 10,993,952 (the "'952 patent"), entitled "STABLE READY TO USE CYCLOPHOSPHAMIDE LIQUID FORMULATIONS" was issued by the U.S. Patent and Trademark Office on May 4, 2021.

6. Each of the Asserted Claims of the '952 Patent is entitled to a priority date of February 15, 2016.

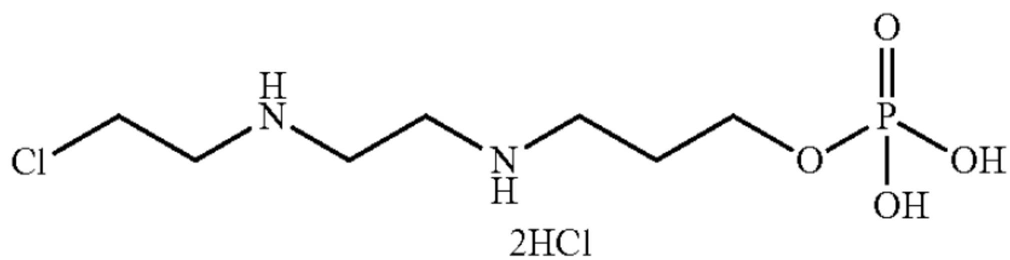
7. Impurity A is bis(2-chloroethyl)amine hydrochloride, and its structure is shown below:



8. Impurity B is 3-(2-chloroethyl)-2-oxo-2-hydroxy-1,3,6,2-oxadiazaphosphonane, and its structure is shown below:



9. Impurity D is 3-[2-(2-chloroethylamino)ethylamino] propyl dihydrogen phosphate dihydrochloride, and its structure is shown below:



III. THE PERSON OF ORDINARY SKILL IN THE ART

10. Accord proposed that a POSA would have had an advanced degree in pharmaceutical sciences, chemistry, medicinal chemistry, materials science and engineering, or a related field, and specific experience in researching and analyzing pharmaceutical formulations, with experience in liquid pharmaceutical stability. Alternatively, a POSA could be an individual with several years of relevant industrial experience, and specific experience related to researching and analyzing pharmaceutical formulations, with experience in liquid pharmaceutical stability. Such a POSA would have understood that the subject matter of the asserted patents may require a

multidisciplinary approach and would have drawn upon not only his or her own skills, but also could have taken advantage of certain specialized skills of others to solve any given problem (for example analytical chemists to help with testing).

11. Ingenus proposed that a person of ordinary skill in the art as of February 2016 includes a person having (i) a B.S. in chemistry or pharmaceutical sciences or a related field and at least six years' experience formulating, characterizing, and/or analyzing pharmaceutical products, (ii) a Master's degree in chemistry or pharmaceutical sciences or a related field and at least four years' experience in formulating, characterizing, and/or analyzing pharmaceutical products, or (iii) a Ph.D. degree in chemistry, pharmaceutical sciences or a related field and at least two years' experience in formulating, characterizing and/or analyzing pharmaceutical products. The POSA would have access to and/or collaborate, as needed, with people in other areas of science, including pharmacology, organic chemistry, drug development, and medical treatment. As described, the person of ordinary skill represents the qualifications of those who were addressing this and similar problems in the pharmaceutical industry in and around February 2016.

12. The parties agree that the POSA definitions are substantively similar and do not affect the opinions given by either party's expert or the outcome of this case, and therefore agree to proceed with Ingenus's proposed POSA definition.

IV. PLAINTIFFS' NDA PRODUCT

13. Ingenus is the holder of New Drug Application ('NDA") No. 212501, which was approved by the Food and Drug Administration ("FDA") for the sale and manufacture of Cyclophosphamide solution for intravenous use ("NDA Product" or "Reference Listed Drug

Product" ("RLD Product")). The active ingredient in Plaintiffs' Cyclophosphamide NDA Product is cyclophosphamide. The FDA approved NDA No. 212501 on July 30, 2020.

V. ACCORD'S ANDA PRODUCT

A. ACCORD'S KNOWLEDGE OF THE' 952 PATENT

14. Accord first became aware of the '952 patent shortly after May 4, 2021.

B. ACCORD'S ANDA PRODUCT

15. By letter dated February 20, 2023 ("Accord's Notice Letter"), Accord notified Plaintiffs that it had filed an Abbreviated New Drug ("ANDA") No. 218250 with a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) that the '952 patent is invalid, unenforceable, and/or will not be infringed by the product that is the subject of ANDA No. 218250 ("Accord's ANDA Product").

16. Through ANDA, No. 218250, Accord seeks approval under section 505(j) of the FDCA to engage in the commercial manufacture and sale of the ANDA Product before expiration of the '952 Patent, to market Cyclophosphamide Injection 200 mg/mL. (2.5 mL, 5 mL, and 10 mL).

REDACT [redacted]

18. Accord's ANDA Products contain cyclophosphamide at a concentration of 12% to 23% based on the total formulation weight.

19. Accord's ANDA Products contain ethanol.

20. Accord's ANDA Products contain polyethylene glycol in an amount of 3.4% to 8.8% based on the total formulation weight.

21. Accord's ANDA Products contain propylene glycol in an amount of 3.4% to 4.4% based on the total formulation weight.

22. Accord's ANDA Products contain a polyethylene glycol to propylene glycol mass ratio of between 1.0:1.0 to 2.0:1.0.

23. The monothioglycerol in Accord's ANDA Products is an antioxidant.

24. The Accord ANDA Products provide the same stability as Plaintiffs' NDA Products.

25. Accord's ANDA products are stable liquid parenteral formulations of cyclophosphamide.

26. Accord's ANDA Products contain 0.01 to 0.02% monothioglycerol based on the total formulation weight.

27. Accord's Product Label instructs that its ANDA Products be administered intravenously.

28. Accord's Product Label contains a Dosage and Administration section which directs that "[d]uring or immediately after the administration, adequate amounts of fluid should be ingested or infused to force diuresis in order to reduce the risk of urinary tract toxicity. Therefore, cyclophosphamide should be administered in the morning."

29. Accord's Product Label contains a Dosage and Administration section which Instructs that "[w]hen cyclophosphamide is included in combined cytotoxic regimens, it may be necessary to reduce the dose of cyclophosphamide as well as that of the other drugs."

30. Accord's Product Label contains a Dosage and Administration section which provides instructions for direct intravenous injection and intravenous infusion.

31. Accord's Product Label contains instructions for use of its proposed product to lactating women, directing that "lactating women [be advised] not to breastfeed during the treatment and for 1 week after the last dose."

32. Accord's Product Label contains instructions for use of its proposed product to pregnant women, directing that "pregnant women and females [be advised] of reproductive potential of the potential risk to the fetus."

33. Accord's Product Label contains instructions for use of its proposed product to geriatric patients, directing that "dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac functioning, and of concomitant disease or other drug therapy."

34. Accord's Product Label contains a Patient Counseling Information Section 17 that advises that patients be informed of certain side effects and toxicities set forth in Section 17.

VI. THE PRIOR ART

U.S. PATENT NO. 4,879,286 TO ALAM *ET AL*. ("ALAM");

35. Alam is prior art to the 952 patent.

36. Alam was considered by the Examiner during prosecution of the 952 patent.

U.S. PATENT APPLICATION PUBLICATION NO. 2015/0320775 TO PALEPU *ET AL*. ("PALEPU")

37. Palepu is prior art to the 952 patent.

38. Palepu was considered by the Examiner during the prosecution of the 952 patent.

<u>WO 2016/005962 TO SHAIK ET AL. (“SHAIK”)</u>

39. Shaik is prior art to the 952 patent.

40. Shaik was not considered by the Examiner during prosecution of the 952 patent.

<u>U.S. PATENT NO. 4,952,575 TO SAUERBIER *ET AL*. (“SAUERBIER”)</u>

41. Sauerbier is prior art to the 952 patent.

42. Sauerbier was considered by the Examiner during prosecution of the 952 patent.

<u>WO 02/02125 TO TAIT *ET AL*. (“TAIT”).</u>

43. Tait is prior art to the 952 patent.

44. Tait was not considered by the Examiner during prosecution of the 952 patent.

EXHIBIT 2

REDACTED PUBLIC VERSION

EXHIBIT 2

PLAINTIFFS' STATEMENT OF ISSUES OF FACT THAT REMAIN TO BE LITIGATED

Pursuant to D. Del. LR 16.3(c)(4), Plaintiffs submit the following statement of contested facts. Plaintiffs have attempted to anticipate issues defendant will raise to the extent possible, but defendant may not raise all of these issues at trial and/or may seek to modify these issues or raise additional issues. Plaintiffs reserve the right to respond to contest any issue raised by defendant. Plaintiffs reserve all rights to supplement/or modify these contested facts in response to the Court's orders and other rulings, or as otherwise appropriate, at or after trial, without amending this pretrial order. In accordance with the Court's guidance, Plaintiffs will provide detailed proposed findings of fact and conclusions of law in posttrial submissions scheduled to be ordered by the court.

To the extent that Plaintiffs' statement of issues of law, which is submitted as **Exhibit 2** hereto, contains issues of fact, those issues are incorporated herein by reference. Likewise, if the Court determines that any issue identified by Plaintiffs as a contested fact is more appropriately considered an issue of law, Plaintiffs incorporate such issue(s) into their disclosures in **Exhibit 4**. By including a fact here, Plaintiffs do not assume the burden of proof or production with regard to the facts that are defendant's burden to prove.

TABLE OF CONTENTS

I. THE INVENTION OF THE ‘952 PATENT 3

II. THE PERSON OF ORDINARY SKILL IN THE ART 3

III. PLAINTIFFS’ NDA PRODUCT 4

IV. ACCORD’S ANDA PRODUCT 5

V. CLAIM CONSTRUCTION 9

VI. INFRINGEMENT BY ACCORD’S ANDA PRODUCTS 12

VII. VALIDITY OF THE ’952 PATENT 17

2. There is no motivation to combine the prior references as Accord has done 26

3. The claimed formulations show surprising and unexpected superiority over the prior art formulations 28

4. Secondary considerations demonstrate the claimed subject matter is nonobvious 33

B. THE TERM “ABOUT” IN THE ’952 PATENT INFORMS A PERSON OF ORDINARY SKILL IN THE ART OF THE SCOPE OF THE CLAIMS 39

C. THE ’952 PATENT DEMONSTRATES THAT THE INVENTOR WAS IN POSSESSION OF THE INVENTION AND ENABLES A PERSON OF ORDINARY SKILL TO MAKE AND USE THE INVENTION 42

I. THE INVENTION OF THE ‘952 PATENT

1. Ingenus is the owner of the ‘952 Patent.

2. The ‘952 patent discloses a stable, ready to use liquid parenteral formulation of cyclophosphamide comprising one or more solvents, and other pharmaceutically acceptable adjuvants, with less than 0.5% of each of impurities A, B, and D measured after a fixed period of time.

3. The subject matter claimed in the 952 Patent was invented over the course of multiple years of continuous work by scientists at plaintiff Leiutis pharmaceuticals.

4. The work leading to the invention of the subject matter claimed in the ‘952 Patent was not routine.

5. Numerous aspects of the inventions of the 952 Patent were unforeseeable, unexpected, and unpredictable.

6. Beginning in 2016, Leiutis undertook extensive research into formulation development in efforts to develop a liquid formulation of cyclophosphamide for injection

II. THE PERSON OF ORDINARY SKILL IN THE ART

7. A person of ordinary skill in the art as of February 2016 includes a person having (i) a B.S. in chemistry or pharmaceutical sciences or a related field and at least six years' experience formulating, characterizing, and/or analyzing pharmaceutical products, (ii) a Master's degree in chemistry or pharmaceutical sciences or a related field and at least four years' experience in formulating, characterizing, and/or analyzing pharmaceutical products, or (iii) a Ph.D. degree in chemistry, pharmaceutical sciences or a related field and at least two years’ experience in formulating, characterizing and/or analyzing pharmaceutical products.

8. The POSA would have access to and/or collaborate, as needed, with people in other areas of science, including pharmacology, organic chemistry, drug development, and medical

treatment. As described, the person of ordinary skill represents the qualifications of those who were addressing this and similar problems in the pharmaceutical industry in and around February 2016.

III. PLAINTIFFS' NDA PRODUCT

9. NDA No. 212501 is directed to Cyclophosphamide 200 mg/mL (500 mg/ 2.5 mL and 1 g/ 5 mL) in a multiple-dose vial. A supplemental dosage form 200 mg/mL (2 g/ 10 ml) was approved November 19, 2021, under New Drug Application No. N212501.

10. Plaintiffs' Cyclophosphamide NDA Product is an injectable solution indicated for the treatment of malignant diseases such as malignant lymphomas (Hodgkin's disease, lymphocytic lymphoma, mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma); multiple myeloma, leukemias (chronic lymphocytic leukemia, chronic granulocytic leukemia, acute myelogenous and monocytic leukemia, acute lymphoblastic (stem-cell) leukemia); mycosis fungoides, neuroblastoma, adenocarcinoma of the ovary, retinoblastoma, and breast carcinoma.

11. Plaintiffs' Cyclophosphamide NDA Product's recommended dosage is 40 mg per kg to 50 mg per kg in divided doses over 2 to 5 days.

12. The '952 patent is listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations ("the Orange Book") in connection with Cyclophosphamide Injection.

13. NDA No. 212501 provides for each of the 2.5 mL, 5 mL, and 10mL presentations to contain Propylene Glycol in an amount of 34.0 mg/mL,

14. In the RLD Product, each of the 2.5 mL, 5 mL and 10 mL presentations contain Polyethylene Glycol in an amount of 34.0 mg/mL.

15. In the RLD Product, each of the 2.5 mL, 5 mL and 10 mL presentations contain Monothioglycerol in an amount of 0.138 mg/mL.

16. In the RLD Product, each of the 2.5 mL, 5 mL and 10 mL presentations contain Dehydrated Alcohol in an amount of 620 mg/mL.

IV. ACCORD'S ANDA PRODUCT

17. Accord's ANDA Product has been developed as generic equivalent to the RLD. The proposed product has the same dosage form as that of the RLD, and is intended for the same indications, dosage regimen and route of administration.

18. Accord's ANDA Product is pharmaceutically equivalent to Plaintiffs' RLD product.

19. The formulation of Accord's proposed Cyclophosphamide Injection 200 mg/mL (2.5 mL, 5mL and 10 mL) product is identical to the Reference Listed Drug (RLD) Cyclophosphamide Injection 500 mg/2.5 mL (200 mg/mL), 1 g/5 mL (200 mg/mL) and 2 g/10 mL (200 mg/mL);

20. Accord's ANDA Product contains the same active ingredient cyclophosphamide USP and all inactive ingredients in the same concentration per unit as that of the RLD.

21. Ms. Sabita Nair, Vice President-Regulatory Affairs for Accord Healthcare Inc. was involved in the preparation and/or filing of Accord's ANDA No. 218250.

22. Accord filed ANDA No. 218250 with a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '952 Patent.

23. Ms. Sabita Nair, Vice President-Regulatory Affairs for Accord Healthcare Inc. and Dr. Alpesh Pathak, Global IP Head for Intas Pharmaceuticals Ltd., were involved in the preparation of Accord's Paragraph IV Certification.

24. Accord considered the RLD and the Orange Book listed patents in making its decision to seek marketing approval from the FDA in connection with ANDA No. 218250.

25. Accord copied the formulations of Plaintiffs' NDA Products in the Accord's ANDA Products.

REDACT [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

REDACT [redacted]

[redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

44. The Accord's ANDA Products provide the same stability as Plaintiffs' NDA Products.

45. Accord's ANDA products are stable liquid parenteral formulations of cyclophosphamide.

46. Accord specific intents to and has intended to cause acts by others constituting direct infringement via its Package Insert instructions.

V. CLAIM CONSTRUCTION

47. The terms "ethanol content of about 70% to about 75%" and "cyclophosphamide in a concentration of about 12% to about 23%" as used in the asserted claims have clear, plain and ordinary meanings that inform a person of ordinary skill in the art of the scope of the asserted claims in U.S. Patent 10,993,952 ("the '952 Patent"). No claim construction is needed for these terms.

48. To the extent the Court deems a construction necessary, "about" should be construed as meaning "approximately"

49. The term "about 70% to about 75%" is recited in independent Claim 1 of the '952 Patent, and by necessity, dependent Claims 2–3.

50. Claim 4 recites "an ethanol content of about 70% based on total formulation weight."

51. Claim 1 also recites "cyclophosphamide in a concentration of about 12% to about 23%" and claim 4 recites "about 23%" cyclophosphamide.

52. The claims recite the ethanol and cyclophosphamide amounts as percentages of total formulation weight, and the term "about" appears not less than 16 times in the claims in addition to the two terms challenged by Accord.

53. Because the same terms appearing in different portions of the claims should be given the same meaning, the repeated use of "about" in other claims informs the construction of "about" in Claim 1.

54. In the specification, "about" is used to describe the solvent content of the formulation. The '952 Patent states "[t]he quantity of solvents ranges from about 40-99% by weight of the composition." col. 3, ll. 29–31. The patent describes the preferred embodiment

of the invention as having as a solvent ethanol (20-98%), while the most preferred embodiment of the invention as having as a solvent ethanol (40-92%). col. 3, ll. 49–67.

55. The Examples disclose ethanol amounts (based on total formulation weight) of 75.9% (Ex. 1), 74.81% (Ex. 2), and 70.58% (Ex. 6).

56. A POSA would understand "about" in reference to an amount or a range as meaning "approximately", and that use of "about" avoids a strict numerical boundary to the specified parameter and that the range should be understood in context. As a matter of pharmaceutical formulation, the word "about" with reference to a value or range is intended to recognize slight batch-to batch variations that inevitably result in the manufacture of pharmaceutical products. Accord's Quality Target Product Profile (QTPP) allows for cyclophosphamide Assay (200 mg anhydrous cyclophosphamide/ml) to be 90.0% - 110.0% of the label claim.

57. The fact that during prosecution, the examiner allowed the claims and stated that formulations of Example 2, Example 6 and the 90:5:5 formulation (containing 69.81% ethanol) were all encompassed by the instant claims, provides further support for "about" permitting a claim scope that goes beyond the fixed endpoints of 70% and 75% as proposed by Accord.

58. In addition, the examiner expressly stated that cyclophosphamide amounts above 23% would be within the scope of a claim reciting that endpoint, stating "the upper limit of cyclophosphamide disclosed in the specific examples of the Specification is 23.25%, 22.62%, 22.52%, which could be interpreted as approx. 23%."

59. The examiner never challenged the use of "about" as indefinite for either the range of the amount of ethanol or the range of the amount of cyclophosphamide.

60. Nowhere did the examiner express concern over the term "about," nor did she reject the claims for including that term. In allowing the asserted claims she specifically relied on the

term "about" in determining that support existed for the allowed claims. She stated: "The amended claims of 23 March 2021 find support in formulations Example 2 and Example 6 of the Specification; the values calculated for the concentrations are rounded: a calculated cyclophosphamide concentration of 22.62% in Example 6 is "about 23%" in claim 46; a calculated concentration of 3.39% propylene glycol in Example 6 is "about 3.4%" in claim 46; a calculated concentration of 4.41% propylene glycol in Example 2 is "about 4.4%" in instant claim 46."

61. In a related case, Ingenus Pharms., Inc. et al. v. Nexus Pharms., Inc., No. 22-cv-2868 (N.D. Il July 31, 2024), the Court rejected a challenge to the "about" terms in Claims 1-4 of the '952 Patent as indefinite, and construed "about" in the '952 Patent claims to mean "approximately." The Court relied on the patent specification and prosecution history, citing the patent examiner's statement that "the upper limit of cyclophosphamide of the specific examples of the patent is 23.25%, 22.62%, 22.52%, which could be interpreted as approximately 23%," the Court concluded that "[t]he examiner understood "about" to mean approximately and understood amounts of cyclophosphamide above 23% to be included within a claim reciting 23% as a numerical endpoint."

62. The examiner understood "about" to mean approximately, and she understood that amounts of cyclophosphamide above 23% to be included within a claim reciting 23% as a numerical endpoint.

63. Even if the weight of cyclophosphamide monohydrate is used to determine the concentration of cyclophosphamide as a percentage of total formulation weight, the 23.7% calculated amount would be within the scope of the claims.

VI. INFRINGEMENT BY ACCORD'S ANDA PRODUCTS

REDACT [redacted]

REDACTED

ACC-CYC0000334-335.

REDACT [redacted]

REDACTED

[redacted]

67. Because the Examiner stated that the 90:5:5 formulation example was covered by the claims, the identical formulation by Accord is also covered by the claims and thus infringes the ‘952 Patent.

[redacted]

71. It is improper to calculate cyclophosphamide concentration based on the amount of cyclophosphamide monohydrate used as a formulation ingredient. In addition to the weight of water that dissociates in solution, the weight of organic components that are not cyclophosphamide would erroneously be included in the calculation.

72. When cyclophosphamide monohydrate is dissolved in ethanol and the other solvents, the monohydrate portion dissociates in solution, leaving cyclophosphamide (200 mg/ mL) as the active ingredient, no longer in hydrated form.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

REDACTED

REDACT [redacted]

79. Accord's proposed ANDA Products contain "an ethanol content of about 70% to about 75% based on total formulation weight" as required by the '952 Patent claims.

REDACT [redacted]

81. While 70% and 75% are numerical ends of the claimed range, the term "about" provides some leeway beyond the strict numerical end points recited.

82. In the specification, "about" is used to describe the solvent content of the formulation, and is not restricted to the numerical endpoints of the range provided. the

specification describes preferred and most preferred lower limits of ethanol as 20% and 40%, respectively. The patent disclosure relating to the ethanol content is keyed to the technologic context of the ability of ethanol, as one of three cosolvents along with PG and PEG, to provide stable formulations as compared to those in the prior art. A person skilled in the art would recognize from a stylistic standpoint that amounts of ethanol below 70% are within the "about 70%" recited in Claim 1.

83. In the field of pharmaceutical formulation, the word "about" with reference to a value or range is intended to recognize slight batch-to-batch variation that results in the manufacture of pharmaceutical products. In Accord's ANDA, the Release Specification for each presentation of the 200 mg/mL product may contain 90% to 110% of the label claim for ethanol content. If approved, Accord may commercialize its products with REDACTED [redacted] which would literally infringe Claim 1 of the '952 Patent.

REDACT [redacted]

[redacted] [redacted]

[redacted] [redacted] would meet the 70% limitation of Claim 1 proposed by Accord. A POSA would know that if a digit to be rounded is greater than 5, then by rounding POSA would add "1" to the last digit to be retained and drop all digits to the right. However, if the digit to be

dropped is less than 5, then by rounding POSA would drop it without adding any number to the last digit. Here A POSA would REDACTED to 70% and thus meet the 70% limitation of Claim 1 proposed by Accord.

REDACT [redacted]

[redacted]

89. The ’952 Patent is listed in the FDA’s orange book, and Accord’s Paragraph IV certification referenced the ’952 Patent when filing its ANDA. Therefore, Accord had knowledge of the patent. Accord’s Package Insert directs its readers to use the infringing product.

90. The Package inserts provide instruction on how to use the accused products by, directing medical professionals to withdraw the prescribed dose from the vial, dilute to a specified concentration, and administer to patients. By providing Package inserts that instruct the use of an infringing product, Accord induces infringement of the ‘932 patent.

VII. VALIDITY OF THE ’952 PATENT

Accord Has Not Shown By Clear and Convincing Evidence That The Asserted Claims of the ‘952 Patent Are Obvious Under § 103

91. The Asserted Claims of the ‘952 Patent would not have been obvious to a POSA at the time of the invention.

92. None of the prior art references identified by Accord, alone or in combination, would have led a POSA to the invention claimed 952 patent with reasonable expectation of success.

93. The scope and content of the prior art relates to formulations of cyclophosphamide including formulation components and methods of stabilizing cyclophosphamide.

94. The differences between the claimed inventions and the prior art are set forth with respect to the particular references relied on by Accord.

a. U.S. Patent No. 4,879,286 to Alam *et al*. (“Alam”);

95. Alam discloses liquid formulations of cyclophosphamide for parenteral administration comprising cyclophosphamide carrier that included about 50-100% polyol, and about 0 to 50% water. Suitable polyols included propylene glycol, polyethylene glycol, glycerol, or combinations thereof, and water.

96. The only claim of Alam recites a cyclophosphamide formulation for parenteral administration comprising a substantially anhydrous carrier having about 80% propylene glycol and about 20% polyethylene glycol. Alam teaches that, in cyclophosphamide liquid formulations, 100% organic vehicle shows unexpected increased stability, and a 80/20 mixture of propylene glycol/polyethylene glycol imparts the most improved stability.

97. Alam does not disclose any 3-solvent systems that include ethanol, propylene glycol, and polyethylene glycol.

98. Alam discloses a Cyclophosphamide concentration of from about 5 mg 2000 mg/mL based on formulation weight, a 200-fold variance. No teaching in Alam directs a POSA to the 12-23% range of cyclophosphamide as claimed.

99. Alam teaches that the desired stability of Cyclophosphamide formulations can be achieved when ethanol is used in an amount of 10 to 30% based on the total formulation weight. 30% is the maximum amount of ethical based on total formulation weight taught by Alam.

100. Alam prepared no ethanol containing formulations and provides no data on the stability of formulations containing ethanol. A POSA text would not understand from Alam the extent to which, if any, the prophetic 10-30% ethanol concentration would stabilize the inventive formulations.

101. The examples of Alam show that the subject formulations are stable at 4^{o}C (refrigerator temperature) for several weeks but show insufficient stability at room temperature or higher. The formulations of Alam would not be suitable as pharmaceutical preparations, and a POSA would not begin with the Alam reference's teachings when improving upon prior art cyclophosphamide Formulations.

102. Alam does not teach a concentration of polyethylene glycol that is greater than the concentration of propylene glycol, and does not teach those two solvents in a 1:1 mass ratio. To the contrary, Alam's disclosure and examples teach a 4: 1 weight ratio of propylene glycol to polyethylene glycol.

103. Alam does not teach Polyethylene glycol concentration of about 3.4% to about 8.8% based on total formulation weight, and does not teach propylene glycol and a concentration of about 3.4 to about 4.4% based on total formulation weight. Examples 10 and 11, the only

examples containing polyethylene glycol and propylene glycol feature concentrations of these solvents Weight ranges over 20% of the total formulation weight.

104. Alam does not teach the use of an antioxidant, and nowhere mentions the use of Monothioglycerol.

105. Alam does not teach or suggest that the disclosed formulations would have reduced amount of impurities A, B, and D below 0.5%, when measured at 40C/75% RH for seven days.

b. U.S. Patent Application Publication No. 2015/0320775 to Palepu *et al*. ("Palepu")

106. The Palepu Reference is generally directed to Formulations of Cyclophosphamide Liquid Concentrate. Disclosed are liquid cyclophosphamide compositions having improved solubility characteristics and enhanced appearance relative to prior art forms.

107. Palepu teaches Cyclophosphamide concentrations ranging from about 100 to about 600 mg/mL.

108. The only solvent systems described in Palepu contain either ethanol and PG; ethanol and PEG; and PEG and PG. The weight ratios of the solvent systems are not given. Three-solvent systems featuring ethanol, PG and PEG are not disclosed.

109. Palepu made and tested the 11 Examples of Alam and concluded that because of degradation, they were not acceptable as commercial products. A POSA aware of Palepu Aware of its criticisms of the Alam formulations as insufficiently stable, and of its comments that they would not be commercially acceptable due to degradation rates.

110. Palepu made and tested cyclophosphamide formulations at a concentration of 500 mg/mL in ethanol/PEG, ethanol/PG, PEG/PG, both with and without citric acid. Palepu published the results in Table 4 and stated that the solution stability was unsatisfactory. Palepu stated that it

is preferable for cancer drugs that degradation not exceed more than 3 to 5% during storage, But none of the solvent combinations reported in Table 4 that criteria.

111. Palepu teaches that the stability data from studies of cyclophosphamide in pure solvents was not satisfactory and that significant degradation was observed when PG and PEG were used as sole solvents.

112. Palepu teaches that when ethanol is used as the only solvent for cyclophosphamide, the data show that a commercially viable product with acceptable levels of degradation would still be difficult to obtain. The only formulation examples Palepu considered to have sufficient stability to be commercially desirable were those containing citric acid.

113. A POSA reading Palepu for its teachings of solvents would not be led to the use of ethanol, propylene glycol, or polyethylene glycol by themselves. Nor would a POSA be led to solid combinations of ethanol with PG, ethanol with PEG, or PG with PEG in solvent ratios ranging from 90:10 to 10:90.

114. Palepu states that a suitable solvent system includes 70% ethanol, 30% PG about 0.5% thioglycerol on a volume per volume basis for solvent. But Palepu neither makes nor tests any solvents according to this system. A POSA reading Palepu has no stability data on which to evaluate formulations containing the proposed 70/30 system.

115. At a 100 mg/mL concentration, Palepu's suitable solvent system may include 63% by weight ethanol, and at a 600 mg/mL concentration, Palepu's suitable solvent system may include 28% by weight ethanol. A POSA reading Palepu as a whole would understand that citric acid is required to provide the necessary stability to ethanolic solvent systems, and that based on total formulation weight, Palepu teaches the use of less than 70% ethanol.

116. The data in table 4 teach away from the use of PG and PEG in a mass ratio of 1:1.

117. PEG and PG are disclosed in amounts of 25% or higher based on total formulation weight and teach away from the use of PG and PEG in the claimed amounts of 3.4% - 4.4% or 3.4% - 8.8%.

c. WO 2016/005962 to Shaik et al. ("Shaik")

118. The Shaik Reference is generally directed to Formulations of Cyclophosphamide and Processes. Shaik discusses the prior art Sauerbier and Alam references In the background section of the specification. Shaik States that neither reference discloses a stable formulation or composition of cyclophosphamide which is stable for a sufficient period of time. A POSA reading Shaik would understand and be informed by Shaik's conclusions about the prior art Alam and Saurbier references.

119. Shaik's liquid formulations of cyclophosphamide may comprise up to 100% by weight of ethanol or may comprise combinations of glycerol with ethanol or propylene glycol with ethanol or polyethylene glycol with ethanol or polysorbate with ethanol or cremophor with ethanol. P. 19. Sahik does not contain any teaching or suggestion of stable liquid parenteral formulations of cyclophosphamide, ethanol, polyethylene glycol and propylene glycol.

120. In examples 1-8 Shaik provides stability data on cyclophosphamide formulations in ethanol as the only solvent. On a weight percentage basis, the exemplified formulations contain about 36% by weight cyclophosphamide and about 63% by weight ethanol.

121. Examples 9 and 10 of Shaik contain lower than 36% cyclophosphamide and lower than 63% by weight ethanol, but no stability data is provided. Examples 11 through 14 show between about 45 or 70% by weight cyclophosphamide, but no stability data is provided.

122. Shaik does not teach the use of PG and PEG in a mass ratio of 1:1, and does not teach the use of PG and PEG in the claimed amounts of 3.4% - 4.4% or 3.4% - 8.8%.

123. Shaik teaches cyclophosphamide amounts and formulations of 36% by weight of the total formulation or more. Shaik does not teach or suggest the use cyclophosphamide in the claimed range of About 12% to about 23%.

124. Shaik does not teach or suggest reduced formation of impurities A, B, and D when tested under the conditions of the '952 patent claims.

d. U.S. Patent No. 4,952,575 to Sauerbier *et al*. ("Sauerbier")

125. Saurbier discloses solutions containing an oxazaphorin dissolved in very high concentrations of ethanol. Example 1 provides a 25% cyclophosphamide solution in 96% ethanol and the Example 2 provides a 25% ifosfamide solution in 96% ethanol. In both examples, ethanol is present in an amount of about 76% by formulation weight, or about 73% by formulation weight accounting for the water Present in the 96% ethanol.

126. Saurbier's Stability data shows that the annual decomposition rate for cyclophosphamide under refrigerated conditions (4^{o}C) is 1.5% while its annual decomposition rate at 20 C is 15%. A POSA reading this date it would find the stability of the formulation stored at room temperature to be unacceptable.

127. Saurbier's Stability data shows that the annual decomposition rate for ifosfamide under refrigerated conditions (4^{o}C) is 0.02% while its annual decomposition rate at 20 C is 0.3%.

128. A POSA reading this data it would find the stability of ifosfamide to be 50-75 times more stable than cyclophosphamide, based on annual degradation rate.

129. Saurbier also teaches that trials carried out with physiological solvents including PG and PEG, the active oxazaphosphorin Ingredient were much less stable and that due to discoloration and degradation, such solutions could not be used as storage stable pharmaceutical

formulations. A POSA reading Saurbier would understand this teaching to be the same as that observed by Palepu, and would be led away from the use of PG and PEG as sole solvents.

130. Saurbier nowhere discloses a three solvent system containing ethanol, PG, and PEG.

131. Saurbier nowhere discloses the use of PG and PEG in a mass ratio of 1:1, and does not teach the use of PG and PEG in the claimed amounts of 3.4% - 4.4% or 3.4% - 8.8%.

132. Saurbier does not teach or suggest reduced formation of impurities A, B, and D when tested under the conditions of the '952 patent claims.

e. WO 02/02125 to Tait *et al*. ("Tait").

133. Tait Is directed to liquid formulations of ifosfamide In the solvent system comprising 35-75% of lower alcohol based on the total weight of the solvent and 25- 65% of polyol based on the total weight of the solvent.

134. Tait States that oxazaphosphorins Subject to degradation by hydrolysis and that ifosfamide is relatively stable by comparison to cyclophosphamide. A POSA aware of this teaching, and aware of the annual decomposition rate data in Saurbier, would not be motivated to look to the teachings of Tait when seeking to stabilize formulations of cyclophosphamide, Particularly where ifosfamide is 50—75 times more stable.

135. In discussing the Saurbier patent, Tait cites drawbacks associated with the use of ethanol as the only solvent. The volatility of ethanol leads to handling problems during manufacture and filling of the product since weight loss, flammability and solvent extraction issues will be greater. Due to the low viscosity and low surface tension of ethanol, syringe and difficulties are also a drawback. A POSA aware of Tait's teachings And those of Palepu that ethanol only

solvent systems were unacceptable, would be led away from Saurbier's use of an ethanol act solvent system containing 76% (or 73%) by weight of ethanol.

136. Tait Observes that the formulations of Alam show insufficient stability at room temperature To be useful as pharmaceutical products.

137. Like Palepu, Tait made and tested several formulations of Alam, including the most preferred formulation. Tait reports that all of the tested Alam formulations unacceptably degraded due to orange color. A POSA aware of the testing of Alams formulations by Palepu and Tait Would be led away from Alam as a reference for its teachings of cyclophosphamide formulations.

138. Tait describes a preferred embodiment of iphosphamide wherein the solvent system is 70% lower alcohol and 30% polyol, in a formulation having 40% by weight of ifosfamide. In this preferred embodiment, ethanol is present in an amount of 42% by weight of the formulation.

139. Examples 1-5 Teach formulations with ethanol contents ranging between 35% and 75% of the total formulation weight. The stability data for all examples Showed each to be stable at the time frames measured, and each are described as preferred formulations by Tait. The concentration of cyclophosphamide for these examples is about 0.01%.

140. Examples 6 -8 Are cyclophosphamide formulations having 40% by weight of cyclophosphamide. As a result, the ethanol content in all examples is 36%.

141. Tait provide stability data for formulations having 75% ethanol based on total formulation weight, only when using cyclophosphamide in concentrations of about 0.1% by weight. When higher concentrations of cyclophosphamide are used, Tait provides stability data only when the ethanol contents are about 36%.

142. Tait nowhere discloses a three solvent system containing ethanol, PG, and PEG.

143. Tait nowhere discloses the use of PG and PEG in a mass ratio of 1:1, and does not teach the use of PG and PEG in the claimed amounts of 3.4% - 4.4% or 3.4% - 8.8%.

144. Tait does not teach or suggest reduced formation of impurities A, B, and D when tested under the conditions of the '952 patent claims.

2. <u>There is no motivation to combine the prior references as Accord has done</u>

145. A POSA would not have selected Alam as a starting point prior art cyclophosphamide formulations. The stability data disclosed therein showed significant degradation at room temperature after a matter of weeks. Subsequently, both Tait and Palepu made and tested the formulations of Alam and concluded that their degradation profile would not have rendered them acceptable as pharmaceutical products. Alam was selected only through the use of hindsight, based on the knowledge of the claims which require ethanol, PG, and PEG as solvents.

146. To the extent Alam would have been considered by a POSA, it teaches away from other references where it discloses an ethanol concentration of 10-30% based on total formulation weight, the use of PG and PEG in a mass ratio of 4:1, and in amounts of over 20% rather than in the claimed amounts of 3.4% - 4.4% or 3.4% - 8.8%. Moreover, Alam was considered by the patent office during prosecution. After repeated projections over its teachings, the examiner allowed the '952 patent claims to issue based on declaration evidence of surprising and unexpected superiority over the formulations of Alam.

147. Tait is directed to ifosfamide, which is many times more stable than cyclophosphamide. A POSA to improve upon cyclophosphamide stability would not be motivated to look at the teachings of a reference based on a compound that is already more stable than cyclophosphamide. To the extent Tait would have been considered by a POSA, its disclosures of low amounts of Ethanol based on formulation weight, high amounts of PG and PEG, 2- solvent

systems only, no disclosure of mass ratios or Formation of impurities A, B and D in amounts less than 0.5% under the conditions specified in the patent are all factors which would have taught away from the combination of Tait with the other named references. Nothing in Tait would have prompted a POSA to modify its teachings Based on any disadvantages of its formulations.

148. Shaik states that Alam and Sauerbier do not disclose stable cyclophosphamide formulations or those which are stable for longer periods of time. A POSA reading Shaik would not combine its teachings with those of Sauerbier. Even if a POSA did choose Shaik as a starting point, Accord has not identified any shortcomings of its formulations requiring improvement. The only basis upon which Accord seeks to modify Shaik is Through the use of hindsight so that its teachings more closely resemble the claims of the 952 patent.

149. A POSA would have had no reason to modify the disclosure of Palepu, directed to liquid cyclophosphamide formulations containing an acidifying agent such as citric acid. Nothing in Palepu disclosed, taught, suggested any drawbacks with its formulations requiring modification or improvement. Even if a POSA were to consider Palepu as a starting point requiring modification, a POSA would not have omitted citric acid or any other acidifying agent which is responsible for the stability of Palepu's formulations. Palepu's requirement of citric acid to stabilize solvent only formulations teaches away from the claim formulations which do not feature citric acid or any other acidifying agent.

150. A POSA Would have been led away from Sauerbier's Ethanol only formulation, given the difficulties associated with manufacturing and syringe ability identified by Tait and the unacceptable degradation of ethanol only formulations identified by Palepu. Given Sauerbier's disparagement of PG and PEG as single solvent systems for cyclophosphamide, a person skilled

in the art seeking to modify its teachings would have no guidance how to do so, absent the impermissible use of hindsight.

151. None of Tait, Palepu, Sauerbier, Alam, or Shaik disclose 3-solvent systems containing ethanol, PG and PEG as recited in the 952 patent claims. None provide stability data on such a 3-solvent system. None provide A POSA with stability data identifying amounts of impurities A, B and D. A POSA reading these references would not be led to a 3-solvent system Based without the use of hindsight, having full knowledge of the ‘952 patent claims.

152. None of Tait, Palepu, Sauerbier, Alam, or Shaik disclose or suggest the amounts of ethanol and cyclophosphamide in the claim ranges along with the low amounts of PG and PEG in the claim ranges. Only through hindsight reconstruction is it possible to arrive at the claimed formulation ranges by selectively cherry picking data points and amounts from these references.

3. <u>The claimed formulations show surprising and unexpected superiority over the prior art formulations</u>

153. For many of the same reasons that there would be no motivation to select or combine the prior art references the way Accord has done, there would be no reasonable expectation of success.

154. None of Accord’s purported prior art references or combinations thereof would have led a POSA to have a reasonable expectation that a formulation according to the claims of the 952 patent would have been unexpectedly superior in terms of stability and impurity formation relative to the asserted prior art. Indeed, the prior art taught away from formulation with ingredient ranges as claimed in the 952 patent.

155. The pharmaceutical arts, including the art of designing a new liquid formulation, is unpredictable. A person of skill in the art would not have viewed the final outcome of the process

of determining a new formulation containing five ingredients within the claimed ranges to be one of a finite number of identified, predictable solutions. There were an infinite number of possible formulations to try, and using different solvents, different solvent amounts, and different excipients (such as antioxidants or stabilizers) and not to mention other formulations of cyclophosphamide, and the data presented in the prior art references was not sufficiently complete for a person of ordinary skill in the art to expect or predict the stability of the claimed formulations.

156. A person of ordinary skill in the art would not have expected success based on the Alam reference, whose formulations were unstable. Even if Alam was followed, it teaches a solvent system comprising mainly propylene glycol, with the remainder being polyethylene glycol. Alam thus teaches away from the claimed use of propylene glycol and polyethylene glycol in amounts ranging from 3.4% to 8.8%, and provides no reasonable expectation of successfully arriving at a stable formulation with such low amounts of polyols.

157. A person of ordinary skill in the art would not have expected success in inventing a formulation having about 70 to about 75% ethanol based upon the teachings of Alam. Alam contains no stability data for ethanol containing formulations, as none were prepared. Alam's teaching that at most -30% ethanol based on total formulation weight- teaches away from the claimed amount of "about 70%" ethanol and does not provide a reasonable expectation of success when using the claimed amount.

158. A person of ordinary skill in the art would not have expected success based on the Tait reference, which teaches 2-solvent systems including 35%-75% of a lower alcohol and 25%-65% of a polyol. Three-solvent systems are not disclosed, and the introduction of a third, undetermined solvent, in an undetermined amount, increases the unpredictability of successfully obtaining the formulation as claimed and the 952 patent. And where a three solvent system is not

disclosed, nothing in Tait suggests that the third solvent would be a polyol, let alone that if it were, the 2 polyol solvents be present in a 1:1 mass ratio.

159. In addition, the use of high amounts of polyol in Tait teaches away from the claimed use of propylene glycol and polyethylene glycol in amounts ranging from 3.4% to 8.8%, and provides no reasonable expectation of successfully arriving at a stable formulation with such low amounts of polyols. Nothing in Tait suggest a reduced impurity formation of impurities A, B, and D under the accelerated testing conditions of the 952 patent. Because Tait is directed to ifosfamide, there is no indication that the same impurities, A, B and D even form when ifosfamide degrades.

160. A person of ordinary skill in the art would not have expected success based on the Palepu reference which requires the addition of citric acid to obtain the stability Palepu considers desirable for pharmaceutical products. To the contrary, the omission of citric acid would provide a person of ordinary skill in the art with an expectation that the resulting formulation would not be sufficiently stable. Like the Tait reference, three-solvent systems are not disclosed In Palepu, and the introduction of a third, undetermined solvent, in an undetermined amount, increases the unpredictability of successfully obtaining the formulation as claimed and the 952 patent.

161. And where a three-solvent system is not disclosed, nothing in Palepu suggests that the third solvent would be a polyol, let alone that if it were, that 2-polyol solvents be present in a 1:1 mass ratio. In addition, the use of high amounts of polyol in Palepu teache away from the claimed use of propylene glycol and polyethylene glycol in amounts ranging from 3.4% to 8.8%, and provides no reasonable expectation of successfully arriving at a stable formulation with such low amounts of polyols.

162. A person of ordinary skill in the art would not have expected success based on the Saurbier reference which teaches the use of an ethanol-only formulation of cyclophosphamide.

Saurbier's teaching that propylene glycol and polyethylene glycol were not suitable as a single formulation solvents would teach away from their combination with ethanol. Based on the data and disclosure of Saurbier, a person of skill in the art would not have reasonably expected success in preparing a formulation containing a second solvent, let alone a third, and would not have selected as those solvents propylene glycol and polyethylene glycol in any event. Nor would a person of ordinary skill in the art have expected to successfully obtain a stable formulation with the low amounts of propylene glycol and polyethylene glycol that are claimed, because Saurbier is silent on their use as co-solvents, and silent on the amount, if any that should be used.

163. Nor would a person of ordinary skill in the art have expected success based on the Shaik reference, which does not contain any teaching or suggestion of stable liquid parenteral formulations of cyclophosphamide, ethanol, polyethylene glycol and propylene glycol.

164. A Person of ordinary skill would not have expected success by adding monothioglycerol in the claimed amount. Alam and Sauerbier do not mention antioxidants or moonothioglycerol. Palepu states that they may be added in concentrations from about one to about 8 mg/mL. Tait states that they may be added for stabilization but does not state what ranges they may be added in and does not state the basis for when an antioxidant would be required.

165. During prosecution of the application that issued as the 952 Patent, the inventors compared claimed formulations to those in the prior art in order to assess stability and measure impurity formation. The inventors performed a side-by-side comparison testing the stability under the claimed set of accelerated conditions, 1 week at 40oC, 75% RH. In particular, formulations of the Alam, Palepu and Fragale references were tested.

166. From the Alam reference, Formulations 1, 7, and 11 were chosen for study.

167. The inventors also selected for comparison formulations 1 and 2 from Table 4 of Palepu for comparison. When comparing the impurity formation of the claimed formulation to those of Alam and palepu, the claimed formulation was the only one in which levels of the three specified impurities A, B and D was below 0.5% at the end of the aging test.

168. During prosecution, the inventors submitted an additional declaration presenting the comparative stability of the inventive formulations with a prior art Palepu formulation. The data showed that total impurity levels for compounds A, B and D were more than three times greater for the Palepu compound then for Example 2 of the '952 patent, and about twice as great when compared to the 90:5:5 example of the claims originally presented to the examiner in an earlier Declaration.

169. Again comparing the inventive formulations to those of Alam, the inventors told the patent office that the side-by-side comparisons demonstrate unexpectedly superior results in terms of much reduced impurities much better stability. The patent office agreed.

170. In a notice of allowance dated March 28, 2021, the patent office Examiner stated with respect to the above declaration that "[t]he results presented in Tables, pages 4-5, Declaration of 15 January 2021, show unexpected stability with the instantly claimed formulations, compared to that achieved with formulations taught by the prior art by Palepu and Alam. Thus, a liquid parenteral formulation of cyclophosphamide of instant claims 46, 49-51 is not rendered obvious by Alam et al. (US 4,879,286) and Palepu et al. (US 2015/0320775)."

171. The examiner added that "such an improvement instability with the instantly claimed liquid parenteral formulation of cyclophosphamide is noteworthy and unexpected."

4. Secondary considerations demonstrate the claimed subject matter is nonobvious

172. There is substantial evidence of objective indicia of nonobviousness that further establishes that the asserted claims of the ‘952 Patent are not invalid for obviousness. There is a nexus between these objective indicia of nonobviousness and the asserted claims of the ‘952 Patent.

a. Long Felt Need

173. The invention claimed in the ‘952 patent satisfied a long-felt need which was recognized, persistent, and not solved by others

174. At the time of filing the application leading to the ’952 Patent, the only IV formulation of cyclophosphamide available at the time was a lyophilized (powder in a vial) formulation of cyclophosphamide by Baxter Healthcare Corporation that required reconstitution with 0.9% sodium chloride injection, USP or sterile water for injection, USP.

175. At the time of filing the application leading to the ‘952 Patent, there were no FDA-approved, ready-to-use (RTU) formulations of cyclophosphamide.

176. Lyophilized and powdered formulations of the prior art have a number of disadvantages associated with their administration. These prior art lyophilized formulations resulted in disadvantageous moisture content after reconstitution with excipients.

177. There is a higher risk of dosing errors associated with having to reconstitute lyophilized powder at the time of use. While the cyclophosphamide in RTU solutions is completely solvated, incomplete dissolution of lyophilized cyclophosphamide can result in a cloudy solution or one containing solid particles or aggregates. If they cannot be solubilized, then the concentration of the solution may differ from the amount specified in the product label.

178. With lyophilized powders, there is a potential risk of emboli and injection site reactions due to the administration of drug particulates to the patient. This happens when undissolved particulates remain after the reconstitution and infusion steps. This is especially the case for cyclophosphamide in powder preparations as crystals formed may be difficult to dissolve Moreover, when reconstituting powdered cyclophosphamide, additional syringe entries into the vial are required, increasing the chance for coring of the rubber stopper and subsequent administration to the patient.

179. When reconstituting powdered cyclophosphamide, additional entries into the drug vial with the syringe are required, leading to an increased risk of contaminating the vial with microorganisms and then administering the microorganisms to the patient. This is especially problematic in patients with a weakened immune system such as patients with cancer receiving chemotherapy.

180. Powdered formulations require a higher number of steps for preparation and a longer preparation time. Moreover, the cyclophosphamide injection powder formulation may require up to 30 minutes for complete dissolution, resulting in long wait times for patients and a delay in care.

181. After reconstitution, a cyclophosphamide powdered solution must be used immediately or within a maximum of 6 days. That is, any reconstituted material not used immediately, must be stored under refrigerated condition (2°C to 8°C = 36ºF to 46°F), but is only stable for up to 6 days.

182. Powdered lyophilized formulations cost more, based on the additional supplies needed for reconstitution and the additional steps required to prepare a reconstituted solution.

183. Chemotherapy drugs, such as cyclophosphamide, are cytotoxic and classified as hazardous drugs, and pose safety risks if workers are exposed to airborne particulates or subsequent surfaces exposures. As a result, there is an increased risk to pharmacy staff and healthcare workers when reconstituting a powdered formulation. In addition, due to an increased pressure in the vial, there is a higher risk of particulate drug matter escaping if too much diluent is used to dissolve the powder, and a pressure gradient occurs. These factors increase the risk of exposing pharmacy staff and other workers to the cytotoxic drug.

184. The RTU formulations of the '952 Patent solved the above drawbacks of powdered or lyophilized cyclophosphamide formulations.

185. With RTU formulations, each vial is pre-formulated and measured, which increases dosing accuracy by reducing the risk of dosing errors that can occur during reconstitution.

186. RTU formulations comply with The Guidelines of the American Society of Health-System Pharmacists (ASHP) on preventing medication errors in hospitals states that medications should be available in ready-to-administer (RTA) packaging so that there is no need for the nurse to make alterations RTA products have been classified as the safest intravenous products. However, while RTU products are not RTA, they still offer benefits as RTA products are not realistic for chemotherapy when the dose is based upon patient-specific factors that vary across patients (e.g., body weight). Thus, RTU formulations are the next best product selection.

187. For RTU formulations, there is no need to reconstitute the product, so there is no risk for any particulate matter to be infused to the patient. In addition, a reduced number of entries into the vial reduces the likelihood of the syringe needle coring the rubber stopper on top of the vial, which lowers the likelihood of administering a piece of rubber to the patient.

188. With RTU formulations, fewer penetrations into the vial are required, leading to less risk of the product becoming contaminated with microorganisms and introducing a microorganism into a patient, especially a patient with a weakened immune system as occurs in patients with cancer and receiving chemotherapy.

189. RTU Formulations involve a single preparation step that reduces preparation time and increases ease-of-use. In addition, RTU formulations are preferred by users and they are easier to learn to use then powdered formulations.

190. RTU formulations have a greater stability and longer shelf life than powdered formulations. In turn, this reduces drug waste and costs in general and specifically for IV formulations of cyclophosphamide.

191. RTU formulations of cyclophosphamide advantageously have a decreased risk of cardiovascular events for patients as compared to lyophilized powder formulations of cyclophosphamide and other medications.

192. RTU formulations of cyclophosphamide advantageously have a decreased risk of infections for patients as compared to lyophilized powder formulations of cyclophosphamide and other medications.

193.

194. RTU solutions have been determined to be cost-effective compared to products needing to be reconstituted. RTU solutions reduce costs by minimizing wasted material and the need for additional supplies required for reconstitution (e.g., reconstitution solution and syringe). These advantages have been specifically highlighted for RTU formulation of cyclophosphamide.

195. With RTU formulations, reduced handling and manipulation of the drug vial reduces the risk of drug exposure to pharmacy staff and healthcare workers.

196. The cyclophosphamide formulations claimed in the '952 Patent met a long-felt need for treatment and pharmacy operations for a safe, storage-stable manner of formulating cyclophosphamide for IV infusion that eliminated the disadvantages of powdered formulations of cyclophosphamide.

197. None of the prior art references Accord relies upon describe formulations that met the need for a safe, storage-stable formulation of cyclophosphamide for IV infusion that eliminated the disadvantages of powdered formulations of cyclophosphamide.

198. Formulation stability in Palepu is achieved not by the solvent system alone, but by the addition of the ethanol-soluble acidifying agent. While the stability of cyclophosphamide in ethanol "appeared to be significantly better compared to the other two solvents," Palepu states that "the ethanol alone data indicated that a commercially viable product with acceptable levels of degradation would still be difficult to attain." Thus, the ethanol soluble acidifying agent is essential to the formulation of Palepu in order to achieve the desired formulation stability. But Palepu did not meet any long felt need because none of its formulations were available or sufficient to meet that need as of February, 2016.

199. A formulation of the Palepu reference was not available until late 2023, when it was approved by FDA and is commercialized by Eugia. Even so, the Eugia formulation contains ethanol as the only solvent, which should be taken into account for patients in whom alcohol intake should be avoided or minimized.

200. Nor were formulations of Alam, Tait, Saurbier or Shaik ever available to meet the the need for a safe, storage-stable formulation of cyclophosphamide for IV infusion that eliminated the disadvantages of powdered formulations of cyclophosphamide.

b. Copying

201. Accord has admitted that it copied the formulations of Plaintiffs' NDA Products in Accord's ANDA Products.

202. Before deciding to copy Plaintiffs' NDA Products, Accord considered three options: (1) Copy the Ingenus formulation and pursue an ANDA under Section 505(j); (2) Independently develop a noninfringing proprietary nonaqueous formula and pursue an NDA under Section 505(b)(2); or (3) develop a stable room-temperature formulation in accordance with products from Baxter and/or Sandoz.

203. Accord also considered independently developing a noninfringing alternative to Plaintiffs pending patent application.

204. Ultimately Accord copied Plaintiffs' product, notwithstanding that other forms of cyclophosphamide were available for copying.

205. For its formulation, Accord copied the same active ingredient used by Ingenus, cyclophosphamide, in the same concentrations as set forth in Plaintiffs' NDA.

206. For its formulation, Accord copied the same inactive ingredients used by Ingenus, ethanol, propylene glycol, polyethylene glycol and Monothioglycerol, in the same amounts as set forth in Plaintiffs' NDA.

c. Nexus

207. Ingenus' NDA Product is coextensive with the claimed invention of the '952 Patent and so there is a nexus between the claims of the '952 Patent and the objective indicia of nonobviousness put forth by Plaintiffs.

208. The formulation of Accord's ANDA Products according to the information provided in its ANDA practices the claims of the 952 patent.

209. The objective indicia of nonobviousness put forth by plaintiff's are tied to its cyclophosphamide injection products, which are the inventions disclosed and claimed in the '952 patent.

210. The solution to the long-felt need in the art for a stable formulation of cyclophosphamide was met by the formulations claimed in the '952 patent, as commercialized by Plaintiffs as their Cyclophosphamide for injection products.

211. The benefits that derive from Plaintiffs' commercial formulations are directly related to the 952 patent claims, which recite specific ingredients in specific ranges For the claimed formulations.

B. THE TERM "ABOUT" IN THE '952 PATENT INFORMS A PERSON OF ORDINARY SKILL IN THE ART OF THE SCOPE OF THE CLAIMS

212. The terms "ethanol content of about 70% to about 75%" and "cyclophosphamide in a concentration of about 12% to about 23%" as used in the asserted claims have clear, plain and ordinary meanings that inform a person of ordinary skill in the art of the scope of the asserted claims.

213. A POSA would understand that while 70% and 75% (and 12% and 23%) are numerical ends of the claimed range, the term "about" provides some scope of claim coverage beyond the strict numerical end points recited.

214. The term "about" appears 16 times in the asserted claims in addition to in connection with the amounts of ethanol and cyclophosphamide. POSA would understand that all instances of "about" should be given the same meaning.

215. A POSA would review the specification and note that "about" is used to describe the solvent content and the cyclophosphamide content of the formulation. In all cases, the solvent content is not restricted to the numerical endpoints of the range provided. the specification provides

descriptive support for amounts of ethanol lower than 70% that are technologically feasible in the invention, including preferred and most preferred lower limits of ethanol as 20% and 40%, respectively.

216. Example 1 contains 75.9% ethanol by weight ("wt."). All of the disclosure relating to the ethanol content is keyed to the technologic context of the ability of ethanol, as one of three cosolvents along with PG and PEG, to provide stable formulations as compared to those in the prior art. A person skilled in the art would recognize from a stylistic standpoint that amounts of ethanol below 70% are within the "about 70%" recited in Claim 1.

217. A POSA would note that the Examples disclose ethanol amounts (based on total formulation weight) of 75.9% (Ex. 1), 74.81% (Ex. 2), and 70.58% (Ex. 6). A POSA would understand in view of the specification that the term "about" in reference to the solvent ranges is to be accorded meaning, and there is ample support in the specification for "about" permitting a claim scope that goes beyond the rigid fixed endpoints of 70% and 75%.

218. A POSA would understand "about" in reference to an amount or a range as meaning "approximately", and that use of "about" avoids a strict numerical boundary to the specified parameter and that the range should be understood in context. As a matter of pharmaceutical formulation, POSAs understand that the word "about" with reference to a value or range is intended to recognize slight batch-to batch variations that inevitably result in the manufacture of pharmaceutical products.

219. In *Ingenus Pharms., LLC v. Nexus Pharms., Inc.*, No. 1:22-cv-02868, 2024 U.S. Dist. LEXIS 135325 (N.D. Il July 31, 2024the court construed "about" in the claim terms "about 70% to about 75% ethanol" and "about 23% cyclophosphamide" to mean ethanol in a

concentration of *approximately* 70% to *approximately* 75% and cyclophosphamide in a concentration of *approximately* 23%.

220. The prosecution history of the '952 patent is consistent with the specification and also evidences that POSA would conclude that the asserted claims are definite.

221. The examiner expressly stated that cyclophosphamide amounts above 23% would be within the scope of a claim reciting that endpoint, stating that the upper limit of cyclophosphamide disclosed in the specific examples of the Specification is 23.25%, 22.62%, 22.52%, which could be interpreted as approx. 23%. This confirms that the examiner understood "about" to mean approximately, but that she understood amounts of cyclophosphamide above 23% to be included within a claim reciting 23% as a numerical endpoint.

222. The examiner never challenged the use of "about" as indefinite for either the range of the amount of ethanol or the range of the amount of cyclophosphamide. In fact, nowhere did the examiner express concern over the term "about," nor did she reject the claims for including that term. In allowing the asserted claims she specifically relied on the term "about" in determining that support existed for the allowed claims.

223. In allowing the asserted claims she specifically relied on the term "about" in determining that support existed for the allowed claims. She stated: "The amended claims of 23 March 2021 find support in formulations Example 2 and Example 6 of the Specification; the values calculated for the concentrations are rounded: a calculated cyclophosphamide concentration of 22.62% in Example 6 is "about 23%" in claim 46; a calculated concentration of 3.39% propylene glycol in Example 6 is "about 3.4%" in claim 46; a calculated concentration of 4.41% propylene glycol in Example 2 is "about 4.4%" in instant claim 46."

224. A POSA would not have concluded that the asserted claims are indefinite because of

the use of the term “about.”

225. Accord cannot prove by clear and convincing evidence that the term “about 70% to about 75% ethanol” is indefinite. The term should be afforded its plain meaning of “approximately,” which encompasses the amount of ethanol in Accord’s formulations.

226. Accord cannot prove by clear and convincing evidence that the term “about 23% cyclophosphamide” is indefinite. The term should be afforded its plain meaning of “approximately” which encompasses the amount of cyclophosphamide in Accord’s formulations.

227. There is no fixed numerical boundary for the term “about;” for a particular measurement, a POSA would determine the applicable error range and understand the scope of “about.” This type of error range determination is standard in the art.

C. THE ’952 PATENT DEMONSTRATES THAT THE INVENTOR WAS IN POSSESSION OF THE INVENTION AND ENABLES A PERSON OF ORDINARY SKILL TO MAKE AND USE THE INVENTION

228. The’ 952 patent specification fully enables and adequately shows possession of the full scope of the claimed subject matter.

229. The experimental section of the ‘952 Patent contains several examples of the claimed stable liquid parenteral formulations of cyclophosphamide. Example 2 discloses a cyclophosphamide formulation within the scope of the claims because it contains 12.00% cyclophosphamide, 8.80% PEG 400, 74.78% ethanol, 4.41% propylene glycol, and 0.0083% monothioglycerol based on total formulation weight.

230. Example 6 discloses a cyclophosphamide formulation within the scope of the claims because it contains 22.62% cyclophosphamide, 3.39% PEG 400, 70.58% ethanol, 3.39% propylene glycol, and 0.016% monothioglycerol based on total formulation weight.

231. Example 8 discloses a cyclophosphamide formulation within the scope of the claims because it contains 22.62% cyclophosphamide, 3.39% PEG 400, 70.13% ethanol, 3.39% propylene glycol, and 0.016% monothioglycerol based on total formulation weight.

232. Examples 2, 6 and 8 show that the patentees exemplified formulations containing 12% - 22.62% cyclophosphamide, 70.13% – 74.78% ethanol, 3.39% - 8.80% PEG, 3.39% - 4.41% propylene glycol and 0.01% - 0.016% monothioglycerol based on total formulation weight.

233. The Patent states that the examples "describe certain specific aspects and embodiments of the present invention and demonstrate the practice and advantages thereof. A POSA reading this disclosure understands that all of the examples describing formulations of the claims would have the advantages thereof, including, e.g., stability and reduced impurity formation controlled within acceptable limits. The Patent also states that "the examples are given by way of illustration only and are not intended to limit the scope of the invention in any manner." A POSA reading this disclosure understands that the scope of the claimed subject matter is not limited by the formulations of the examples, and would not understand that the claims are limited to the formulation of only those examples wherein stability data is provided.

234. The examples of the '952 Patent enable a POSA to determine whether a given claimed formulation will meet the "stable" limitation for all claims. The '952 Patent states that cyclophosphamide formulations prepared according to the invention *were tested for stability* under accelerated conditions for a period of 1 week at 40° C./75% RH. The *stability data of the invention formulation* is summarized in table 1.

235. The data in Table 1 reports on the stability of formulation Examples 2, 4 and 5 after an accelerated aging study (carried out at 40°C, 75%RH, 7 days) was used to determine the amount and type of certain impurities after a period of time. Because the stability data of Table 1 is reported

for formulations *of the invention*, POSA could thus determine that a given claimed formulation meets the "stable" limitation for all claims.

236. The '952 Patent also describes a number of aspects of stability that would guide POSA to know whether a given claimed formulation will meet the "stable" term for all claims.

237. These portions of the specification relate to: (1) controlling impurities within acceptable limits (2) having less than 0.5% of impurities A, B and D; (3) storage stability after testing at 40ºC, and 75%RH for 7 days ; and (4) stability when stored at 2-8ºC. All of these portions of the specification enable POSA to determine whether a claimed liquid parenteral formulation of cyclophosphamide will meet the "stable" limitation for all claims.

238. In particular, A POSA could test a given formulations for stability after being stored at 40˚ C., 75% RH for 7 days." If the formulations show less than 0.5% each of impurities A, B and D, the formulations would be considered "stable" in accordance with the claims of the '952 Patent.

239. Alternatively, or in combination POSA could store the given formulations at 2° C. to 8° C. as the inventive compositions of Cyclophosphamide were found to be stable when stored at within such a temperature range.

240. During prosecution, the inventors submitted a declaration presenting the comparative stability of the inventive formulations, Example 2, Example 6 and the 90:5:5 formulation submitted in an earlier declaration, as shown below:

Example numbers	Ex-02		Ex-06		90:5:5 (EtOH:PEG400:PG)	
Ingredient	Conc	%w/w	Conc	%w/w	Conc	%w/w
Cyclophosphamide	1 gm	12.01	1 gm	22.62	0.2 g	**22.52**
Dehydrated ethanol	6.23 gm	74.81	3.12 gm	70.58	0.62 g	69.81
PEG400	0.73 gm	8.77	0.15 gm	3.39	0.034 g	3.83
Propylene glycol	0.367 gm	4.41	0.15 gm	3.39	0.034 g	3.83
Monothioglycerol	0.69 mg	0.0083	0.69 mg	0.0156	0.138 mg	0.02

241. The applicants told the examiner that the newly added claim range was supported and spanned by examples 2 and 6 of the specification as shown below:

Ingredient	Ex-02	Ex-06	Claimed Range
	%w/w	%w/w	
Cyclophosphamide	12.01	22.62	12% - 23 %
Dehydrated ethanol	74.81	70.58	69.5% - 76.5%
Polyethylene glycol	8.77	3.39	3.25% - 8.85%
Propylene glycol	4.41	3.39	3.25% - 8.85%
Monothioglycerol	.0083	.0156	0.0075% -0.02%

242. The amounts of formulation ingredients and example 2 and 6 encompass the entire claim range if not nearly the entire claimed range for each ingredient. Thus, exemplary data of stability was provided to the patent office for the entire claimed range, teaching a POSA that any formulation of the claims within the ranges recited would be stable according to the test method described in the patent.

243. When comparing these examples to those of the prior art Alam and Palepu formulations, The inventors told the patent office that the side-by-side comparisons demonstrate unexpectedly superior results in terms of much reduced impurities much better stability.

244. The patent office agreed. In a notice of allowance dated March 28, 2021, the patent office Examiner First stated that example 2, example 6, as well as the 90:5:5 formulation were "all encompassed by the instant claims."

245. The examiner concluded that the results presented in the Declaration of 15 January 2021 showed unexpected stability with the instantly claimed formulations, compared to that achieved with formulations taught by the prior art by Palepu and Alam, and that a liquid parenteral formulation of cyclophosphamide of instant claims was not rendered obvious by Alam and Palepu.

246.

EXHIBIT 3

ACCORD'S PROPOSED FINDINGS OF FACT

REDACTED PUBLIC VERSION

I. SUMMARY OVERVIEW OF ACCORD'S PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW 1

II. BACKGROUND 2

A. THE PATENT-IN-SUIT 3

B. THE PROSECUTION HISTORY 5

C. ASSERTED CLAIMS 9

D. PERSON OF ORDINARY SKILL IN THE ART 10

III. CLAIM CONSTRUCTION/INDEFINITENESS 11

IV. ALLEGED INFRINGEMENT 12

V. FACTS UNDERLYING THE OBVIOUSNESS INQUIRY 13

A. THE SCOPE AND CONTENT OF THE PRIOR ART 13

1. Alam (1989) 13

2. Sauerbier (1990) 16

3. Palepu (2015) 17

4. Shaik (2016) 21

5. Tait (2002) 23

B. DIFFERENCES BETWEEN THE PRIOR ART AND THE CLAIMS AND LEVEL OF SKILL IN THE ART 25

C. OBJECTIVE INDICIA 28

1. Alleged unexpected results 28

2. Alleged long-felt need 30

VI. FACTS RELATED TO LACK OF WRITTEN DESCRIPTION AND ENABLEMENT UNDER 112 30

ACCORD'S PROPOSED FINDINGS OF FACT

Accord submits these Proposed Findings of Fact. To the extent that any finding of fact proposed below is more properly considered a conclusion of law, it should be so considered, and vice versa. Accord may prove any matter identified in the reports of its expert witness and intends to present at trial such additional support contained in its expert's reports regarding the non-infringement and invalidity of the asserted claims of the patents-in-suit that are not expressly set forth herein. Accord reserves the right to supplement these Proposed Findings of Fact, as necessary, including in response to any of Plaintiffs' assertions, and to conform to the evidence presented at trial.

I. SUMMARY OVERVIEW OF ACCORD'S PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW

1. Accord contends that it does not infringe claims 1-4 of U.S. Patent No. 10,993,952 (952 patent) and that the claims are invalid under 35 U.S.C. § 103 and/or § 112.

2. Accord contends that its ANDA product does not infringe any claim of the 952 patent because Accord's ANDA product does not contain "about 70%" or "about 70%-75%" ethanol as required by independent claims 1 and 4 respectively.

3. Accord further contends that the asserted claims are indefinite because it is not reasonably certain what the scope of "about 70%" or "about 70% to about 75%" encompasses.

4. Accord further contends that the claims are obvious over the prior art which taught the use of the claimed solvents to form stable liquid cyclophosphamide formulations and arriving at the claimed invention required only routine optimization of the prior art.

5. Accord further contends that the claims lack written description support and are not enabled because the specification does not demonstrate that the inventors were in possession of or

enabled the full scope of the claims, as the claims are supported by stability testing for only a single example.

II. BACKGROUND

6. Cyclophosphamide is the generic name for 2-[bis(2-chloroethyl)amino]tetrahydro-2H-1,3,2-oxazaphosphorine-2oxide monohydrate. E.g., Alam (DTX-003) at 1:5-7. Cyclophosphamide has long been used in chemotherapy to treat cancers, specifically as an antineoplastic drug and was first disclosed and claimed in 1962. Alam at 1:7-48. Historically, cyclophosphamide was available in parenteral dosage formulations consisting of sterile packaged dry powder blends, which had to be dissolved in water prior to use. Alam at 1:53-57. However, the aqueous solution was only stable for a few hours and would quickly deteriorate. Alam at 1:57-67. In 1985, R.L. Alexander patented a method of freeze-drying cyclophosphamide in a procedure known as lyophilization, which had been commonly used previously with other poorly water-soluble drugs. Alam at 2:13-22. However, lyophilization is costly, inefficient, and can be dangerous. Alam at 2:33-35. Specifically, it requires sophisticated vacuum pumps and other equipment. Alam at 2:36-44. Lyophilization is also inefficient in that time is spent freeze-drying the product and then reconstituting it when needed for use. Alam 2:45-51. Finally, reconstitution exposes the personnel responsible to the agent, which can be dangerous. Alam 2:52-67.

7. Stable liquid cyclophosphamide formulations were thus preferred, and were developed in the prior art, using organic solvents including ethanol, polyethyelen glycol (PEG) and propylene glycol (PG). *See infra*, The Scope and Content of the Prior Art. The art taught that ethanol provides the most stability but that cyclophosphamide was also soluble in PEG and PG and the use of these as co-solubilizing agents avoided handling and manufacturing drawbacks associated with pure ethanol. *See infra*, The Scope and Content of the Prior Art.

A. The Patent-in-Suit

8. U.S. Patent No. 10,993,952 (the "952 patent," DTX-001), entitled "Stable Ready to Use Cyclophosphamide Liquid Formulations," issued on September May 4, 2021 from U.S. Patent Application No. 15/551,507, filed on February 15, 2016. *See* 952 patent, Cover Page. The 952 patent is not entitled to claim priority to any date earlier than February 15, 2016.

9. The 952 patent generally covers pharmaceutical compositions comprising pharmaceutical grade cyclophosphamide meeting certain stability requirements. The specification describes the invention as providing "stable ready to use, liquid parenteral formulations of Cyclophosphamide and process of preparation thereof." 952 patent at 1:6-8. The specification describes a broad range of solvent systems as being preferred, and even most preferred, embodiments:

The preferred embodiment of stable liquid parenteral formulation of Cyclophosphamide comprises:

(i)	Cyclophosphamide	5-40%
(ii)	Polyethylene glycol	0-30%
(iii)	Ethanol	20-98%
(iv)	Propylene glycol	0-20%
(v)	Optionally other pharmaceutically acceptable adjuvants thereof.	

The most preferred embodiment of stable ready to use, liquid parenteral formulation of Cyclophosphamide comprises:

(i)	Cyclophosphamide	6-30%
(ii)	Polyethylene glycol	0-25%
(iii)	Ethanol	40-92%
(iv)	Propylene glycol	0-15%

-continued

(v)	Water for Injection	0-20%
(vi)	Antioxidant	<3%

952 patent at 3:49-4:5.

10. The specification provides 8 example formulations, but includes stability data with respect to the claimed impurities for only example formulations 2, 4, and 5. *See* Table 1. Examples 4 and 5 plainly fall outside the scope of every claim of the 952 patent since neither Example 4 nor Example 5 includes propylene glycol.

11. Example 2 – the only disclosure in the 952 patent of stability data for a formulation that appears to be encompassed by the claims – includes 1.0 g cyclophosphamide, 0.733 g PEG 400, 6.23 g ethanol, 0.367 g propylene glycol, and 0.69 mg monothioglycerol. The ingredient amounts of Example 2 equate to 12.00% cyclophosphamide, 8.80% PEG 400, 74.78% ethanol, 4.41% propylene glycol, and 0.0083% monothioglycerol based on total formulation weight.

B. The Prosecution History

12. During prosecution of the 952 patent, the applicant amended the claims multiple times to narrow the required ethanol content. In particular, certain original claims required ethanol without any limit to the concentration and other claims limited the ethanol content to 20-98% w/w. See, e.g., DTX-002, ING00000444-45. The applicant later introduced claims requiring an ethanol content of 40-92%. See, e.g., ING00000222. After multiple rejections, the applicant later submitted new claims that recited an ethanol content of "about 69.5%-about 76.5%." ING00000077. The applicant cited to Examples 2 and 6 from the specification as support for these new claims. ING00000079. Later, following another examiner interview where the examiner expressed concerns regarding support for the claimed range, the applicants filed a supplemental amendment on March 23, 2021 to further narrow the claimed ethanol content to "about 70% to about 75%." ING00000035, ING00000069.

13. The Examiner also rejected the then-pending claims as being anticipated and or obvious over Alam and Palepu. For example, the Examiner stated:

> It would have been obvious for a person of ordinary skill in the art before the effective filing date of the claimed invention to combine the teachings of Palepu and Alam to arrive at the instant invention. The person of ordinary skill in the art would have been motivated to vary the relative amount of ethanol, propylene glycol, and/or polyethylene glycol in a liquid parenteral formulation of cyclophosphamide, because Alam teaches very good stability for formulations in which cyclophosphamide is dissolved in propylene glycol and/or polyethylene glycol, with additional 10-30% ethanol, Palepu teaches very good stability for formulations in which cyclophosphamide is dissolved in ethanol, and Palepu also evaluates the stability for formulations in which cyclophosphamide is dissolved in 50:50 mixtures of ethanol and polyethylene glycol or propylene glycol stabilized with thioglycerol. Thus, a person of ordinary skill in the art would have explored different relative amounts of ethanol, propylene glycol and/or polyethylene glycol in a liquid parenteral formulation of cyclophosphamide, with the expectation that the resulting formulations will retain therapeutic effect. Such an exploration of different relative amounts of solvents ethanol, propylene glycol and/or polyethylene glycol, in a formulation of cyclophosphamide, with the aim of

> optimizing the stability of the formulation /minimizing the level of impurities in the formulation, is well within the skill of the artisan.

ING000000271.

14. In addition to the narrowing of the claims during prosecution, the applicant submitted a series of inventor declarations attempting to overcome the Examiner's rejection. Eventually, the inventors submitted declarations purporting to test the formulations of Example 2 and a "90:5:5" formulation not disclosed in the specification (which the inventor declarants appear to suggest is similar to Example 6) to examples from Alam and Palepu. One inventor declarant described the example formulations as comprising:

Example numbers	Ex-02		Ex-06		90:5:5 (EtOH:PEG400:PG)	
Ingredient	**Conc**	**%w/w**	**Conc**	**%w/w**	**Conc**	**%w/w**
Cyclophosphamide	1 gm	12.01	1 gm	22.62	0.2 g	**22.52**
Dehydrated ethanol	6.23 gm	74.81	3.12 gm	70.58	0.62 g	69.81
PEG400	0.73 gm	8.77	0.15 gm	3.39	0.034 g	3.83
Propylene glycol	0.367 gm	4.41	0.15 gm	3.39	0.034 g	3.83
Monothioglycerol	0.69 mg	0.0083	0.69 mg	0.0156	0.138 mg	0.02

The declaration also reported the following example formulations from Alam and Palepu:

**HIGHLY CONFIDENTIAL –
SUBJECT TO PROTECTIVE ORDER**

	Palepu formulations		**Alam formulations**					
	Palepu (Mar'19) response		**Formulation 1**		**Formulation 7**		**Formulation 11**	
Ingredient	Conc	%w/w	conc	%w/w	conc	%w/w	conc	%w/w
Cyclophosphamide	550 mg	55	5 mg/ml	0.49	20 mg/ml	1.83	100mg/ml	9.31
Dehydrated ethanol	Qs to 1ml	qs to 100%	-	-	-	-		
PEG400	-		-	-	-	-	19.9	19.9
Propylene glycol	-	-	250 mg/ml	24.48	250 mg/ml	22.89	Qs to 100	Qs to 100
Water for injection	-	-	Qs to1ml	Qs to 100	Qs to1ml	Qs to 100		
Monothioglycerol	-	-			-	-		
Calcium chloride dihydrate	2 mg	0.2			-	-		
Citric acid	11 mg	1.1			-	-		
Glycerol					250mg/ml	22.89		

The declaration then compared the impurity levels following 1 week at 40° C for Example 2, the "90:5:5" formulation, and the prior art formulations:

Parameter	Ex-02		90:5:5 (EtOH:PEG400:PG)		Palepu	
	Initial	1Week 40°C	initial	1 week 40° c	Initial	1Week 40°C
%assay	101.6	101.9	100.4	97.1	102.4	95.8
%ImpA	ND	ND	0.02	0.05	ND	0.33
%ImpB	0.06	0.18	0.04	0.22	0.06	0.23
%ImpD	ND	ND	0.02	0.12	0.01	0.79
%Total imp	0.07	1.87	0.08	3.55	0.11	*7.29
	Increase in impurities to 1.87%		Only 3.3% drop in assay Increase in total impurities to 3.55%		6.6% assay difference Increase in total impurities to 7.29%	

Note: Total impurities is the sum of imp A, imp B, imp C and other impurities.

	EX-02		90:5:5		Alam formulations					
					Formulation 1		Formulation 7		Formulation 11	
Parameter	Initial	1Week 40°C	initial	1 week 40 °C	Initial	1WK 40°C	Initial	1WK 40°C	Initial	1WK 40°C
%assay	101.6	101.9	100.4	97.1	94.8	56.2	100.8	41.2	93.8	87
%ImpA	ND	ND	0.02	0.05	ND	2.74	0.03	2.98	ND	ND
%ImpB	0.06	0.18	0.04	0.22	0.54	ND	0.98	0.95	0.12	0.74
%ImpD	ND	ND	0.02	0.12	ND	ND	ND	39.48	ND	ND
%Total imp	0.07	1.87	0.08	3.55						

ING00000085-89.

15. The Examiner allowed the claims because she concluded:

> Applicant has shown (Tables, pages 4-5, Declaration of 15 January 2021) that better stability (less drop in % assay and less impurities formed after 1 week at 40 °C) is achieved with liquid parenteral formulations of cyclophosphamide (Example 2, and formulation 90:5:5) containing ethanol (70% or 75%), polyethylene glycol and propylene glycol in mass ratio 2 :1 or 1:1, present in concentrations within the instantly claimed ranges,
> compared to liquid cyclophosphamide formulations containing cyclophosphamide dissolved in ethanol (taught by Palepu),
> or compared to cyclophosphamide liquid formulation of cyclophosphamide containing propylene glycol and water (Alam formulation 1); propylene glycol, glycerine and water (Alam formulation 7); or cyclophosphamide dissolved in polyethylene glycol and propylene glycol in a mass ratio of 1 : 4 (Alam, formulation 11).
>
> The results presented in Tables, pages 4-5, Declaration of 15 January 2021, show unexpected stability with the instantly claimed formulations, compared to that achieved with formulations taught by the prior art by Palepu and Alam. Thus, a liquid parenteral formulation of cyclophosphamide of instant claims 46, 49-51 is not rendered obvious by Alam et al. (US 4,879,286) and Palepu et al. (US 2015/032075).

ING00000032.

16. As discussed below, the Examiner erred in finding these results unexpected.

C. Asserted Claims

17. Plaintiffs are asserting claims 1-4:

Claim	Text of Asserted Claim
1	A stable liquid parenteral formulation of cyclophosphamide comprising i) cyclophosphamide in a concentration of about 12% to about 23% based on total formulation weight; ii) an ethanol content of about 70% to about 75% based on total formulation weight;

	iii) both polyethylene glycol and propylene glycol, wherein a polyethylene glycol to propylene glycol mass ratio is between approximately 1.0:1.0 to approximately 2.0:1.0; and iv) about 3.4% to about 8.8% based on total formulation weight of polyethylene glycol v) about 3.4% to about 4.4% based on total formulation weight of propylene glycol vi) wherein, after storage for 7 days at 40° C./75% RH, decomposition to form any of the following impurities is less than 0.5%: a) bis(2-chloroethyl)amine hydrochloride; b) 3-(2-chloroethyl)-2-oxo-2-hydroxy-1,3,6,2-oxadiazaphosphonane; and c) 3-[2-(2-chloroethylamino)ethyl amino] propyl dihydrogen phosphate dihydrochloride.
2	The formulation of claim 1, further comprising an antioxidant.
3	The formulation of claim 2, wherein the antioxidant is monothioglycerol at concentration of about 0.01% to about 0.02% by total formulation weight.
4	A stable liquid parenteral formulation of cyclophosphamide comprising i. cyclophosphamide in a concentration of about 23% based on total formulation weight ii. an ethanol content of about 70% based on total formulation weight; iii. both polyethylene glycol and propylene glycol, wherein a polyethylene glycol to propylene glycol mass ratio is about 1.0:1.0; and iv. about 3.4% to about 8.8% based on total formulation weight of polyethylene glycol v. about 3.4% to about 4.4% based on total formulation weight of propylene glycol, and vi. about 0.02% based on total formulation weight of monothioglycerol

D. Person of Ordinary Skill in the Art

18. Accord submits that a POSA is a person who has

> an advanced degree in pharmaceutical sciences, chemistry, medicinal chemistry, materials science and engineering, or a related field, and specific experience in researching and analyzing pharmaceutical formulations, with experience in liquid pharmaceutical stability. Alternatively, a POSA could be an individual with several years of relevant industrial experience, and specific experience related to researching and analyzing pharmaceutical formulations, with experience in liquid pharmaceutical stability.

19. Ingenus submits that a POSA is:

> a person having (i) a B.S. in chemistry or pharmaceutical sciences or a related field and at least six years' experience formulating, characterizing, and/or analyzing pharmaceutical products, (ii) a Master's degree in chemistry or pharmaceutical

> sciences or a related field and at least four years' experience in formulating, characterizing, and/or analyzing pharmaceutical products, or (iii) a Ph.D. degree in chemistry, pharmaceutical sciences or a related field and at least two years' experience in formulating, characterizing and/or analyzing pharmaceutical products.

20. The parties' definitions of a POSA are not materially different and do not affect any issue in the case. Accord's expert, Dr. Jason McConville, meets or exceeds the definition of a POSA, under either party's definition.

III. CLAIM CONSTRUCTION/INDEFINITENESS

21. Claim 1 of the 952 patent requires "an ethanol content of about 70% to about 75% based on total formulation weight" and claim 4 requires "an ethanol content of about 70% based on total formulation weight." Claim 1 also requires "cyclophosphamide in a concentration of about 12% to about 23%" and claim 4 requires "about 23%" cyclophosphamide. Further, "about" is used with numerous other components recited in the claims.

22. The claims of the 952 patent are entirely unclear what range is covered by "about" and a POSA is left to subjectively guess what is encompassed by the claims.

23. The specification does not provide guidance on the meaning of "about" in the context of the claims as it doesn't use the term "about" to describe the ranges. It uses the term "about" only twice in unrelated contexts, neither of which provide guidance. The specification does not identify which example(s) correspond with the claims. During prosecution, the applicant and examiner referred to only Examples 2 and 6 as being encompassed by the claims.[1] The examples thus do not identify the outer bounds of "about."

---

[1] Accord notes that Example 6 does not contain stability data, and thus does not fall within the scope of the claims, but only within the scope of the solvent limitations.

24. The prosecution history does not clarify the scope of "about." During prosecution, the examiner raised concerns about then-pending claims reciting "about 69.5% to about 76% ethanol" as not having support in the specification, and the applicant amended the claim to its current "about 70% to about 75%."

IV. ALLEGED INFRINGEMENT

REDACT [redacted]

REDACTED

REDACTED

27. Claim 1 requires "an ethanol content of about 70% to about 75% based on total formulation weight" and Claim 4 requires "an ethanol content of about 70% based on total formulation weight." REDACTED which is not "about 70% to about 75%" or "about 70%" under any reasonable construction.

28. Claim 4 requires "cyclophosphamide in a concentration of about 23% based on total formulation weight." REDACTED is not "about 23%" under any reasonable construction.

V. FACTS UNDERLYING THE OBVIOUSNESS INQUIRY

29. Invalidity is assessed from the perspective and knowledge of a POSA at the time of the alleged invention of the asserted patents. The earliest effective filing date for the asserted claims is February 15, 2016.

A. The Scope and Content of the Prior Art

30. The prior art includes the following published references and the general knowledge of a POSA.

1. Alam (1989)

31. U.S. Patent No. 4,879,286 ("Alam", DTX-003) is prior art to the asserted patents under 35 U.S.C. § 102(a)(1) because it was published in 1989, before the earliest possible effective filing date of February 16, 2015.

32. In short, Alam generally teaches that liquid cyclophosphamide is more stable in purely organic solvents, including combinations of PEG and PG. Alam teaches that ethanol would be expected to provide stability, but does not investigate the use of ethanol.

33. Alam teaches a cyclophosphamide formulation that "comprise[s] a solution of cyclophosphamide with an organic polyol as cosolvent, which provide enhanced shelf-life and greater ease of administration." Alam at Abstract. Alam teaches that "a 100% organic vehicle show unexpectedly increased stability." Alam at 4:38-39. Alam teaches that the "organic polyols which are useful in the present invention include propylene glycol, polyethylene glycol, glycerol, and mixtures thereof." Alam at 3:59-61.

34. Alam teaches that these formulations provide "a number of important advantages" because the "liquid formulations provide a simple method of dosing"; "[n]o reconstiutiton is necessary"; and "[c]yclophosphamide has greater solubility in the liquid carrier used in the present formulations" and thus "the concentration of cyclophosphamide in the formulations of the present invention can be as high [as] 1000 mg/ml whereas the highest concentration achievable with water is only 33 mg/ml" and "consequently, less volume of solution needs to be injected into the patient for administering the same amount of the drug." Alam at 4:49-60. Alam further teaches that these advantages "include increased safety by virtue of the decreased amount of manipulation by, and hence exposure to, clinicians, of the active agent; increased assurance of sterility; and decreased likelihood of errors in dosing." Alam at 4:61-66.

35. Alam prepares eleven formulations which it lays out in Table 1[2]:

[2] Tables herein have been edited for readability to remove stray marks or connect tables that spanned page breaks.

HIGHLY CONFIDENTIAL –
SUBJECT TO PROTECTIVE ORDER

TABLE 1

	CYCLOPHOSPHAMIDE FORMULATIONS										
Example	1	2	3	4	5	6	7	8	9	10	11
Propylene Glycol	25%		25%		25%		25%		50%	80%	80%
Polyethylene Glycol										20%	20%
Glycerol		25%	25%			25%	25%		50%		
Water for Injection	75%	75%	50%	100%	75%	75%	50%	100%			
Cyclophosphamide (mg/ml)	5	5	5	5	20	20	20	20	20	20	100

Alam at Table 1 (column 5).

36. Alam provides stability data, as shown in tables 2-5, showing the best stability for Examples 9-11 which contain no water, and combinations of PG and PEG or PG and glycerol:

TABLE 2

	PERCENT CYCLOPHOSPHAMIDE (4° C.)					
Example	Zero Time	1 Week	2 Weeks	9 Weeks	11 Weeks	15 Weeks
1	100	96.0	93.8			
2	100	96.8	93.7			
3	100	96.8	92.5			
4	100	97.2	94.8			
5	100	99.4	96.4		73.1	
6	100	97.8	94.7		71.0	
7	100	99.1	96.8		73.4	
8	100	97.7	95.0		87.0	70.8
9	100	99.4	99.3		96.2	
10	100	99.2	98.5		98.7	
11	100		99.4	97.3		

TABLE 3

PERCENT CYCLOPHOSPHAMIDE (ROOM TEMPERATURE)					
Example	Zero Time	1 Week	2 Weeks	9 Weeks	11 Weeks
1	100	83.5	71.7		
2	100	80.8	70.2		
3	100	84.8	73.7		
4	100	81.4	69.6		
5	100	83.3	72.2		
6	100	81.5	70.8		
7	100	85.6	76.1		
8	100	81.8	70.5	0.1	
9	100	97.6	94.1	74.4	
10	100	98.9	97.1	86.6	
11	100	96.7	88.0		

37. Alam also teaches "it is likely that the desired stability of cyclophosphamide will also be achieved with the formulations of the present invention in combination with alcohols such as ethanol." Alam at 4:43-47.

2. Sauerbier (1990)

38. U.S. Patent No. 4,952,575 ("Sauerbier", DTX-009) is prior art to the asserted patents under 35 U.S.C. § 102(a)(1) because it was published in 1990, prior to the earliest possible priority date for the asserted patents of February 16, 2015.

39. Sauerbier teaches liquid parenteral cyclophosphamide formulations using 96% ethanol and that its formulations have greatly improved stability over aqueous solutions:

Annual Decomposition Rate	In Water	In 96% Ethanol
Cyclophosphamide at 4° C.	25%	1.5%
Cyclophosphamide at 20° C.	97%	15.0%
Ifosfamide at 4° C.	2%	0.02%
Ifosfamide at 20° C.	20%	0.3%

40. Sauerbier teaches examples of specific formulations, for example combining 6 liters of 96% ethanol with 2.673 kg of cyclophosphamide monohydrate. Sauerbier at 4:40-61.

3. Palepu (2015)

41. U.S. Patent Publication No. 2015/0320775 ("Palepu", DTX-004) is prior art to the asserted patents under either 35 U.S.C. § 102(a)(1) because it was published November 12, 2015, prior to the filing date of February 15, 2016.

42. In short, Palepu teaches forming stable cyclophosphamide solutions at very high concentrations using ethanol as a primary solvent and acidifying agents such as citric acid or calcium chloride. Palepu further teaches other solubilizing agents such as PG may be used in smaller amounts.

43. Palepu teaches example cyclophosphamide liquid formulations at several cyclophosphamide concentrations. For example, Palepu states:

> The concentration of the cyclophosphamide in the inventive solutions prior to dilution and administration to patients is in many aspects from about 100 to about 600 mg/ml, or from about 250 to about 550 mg/ml. In other preferable embodiments, the cyclophosphamide concentration is about 200, 400 or 500 mg/ml. Such aspects of the invention are for storage purposes typically. As will be understood by those of ordinary skill, the highly concentrated alcohol-based

> compositions will typically undergo significant dilution prior to IV or parenteral administration to a patient in need thereof.

Palepu at [0015].

44. Palepu further teaches that the:

> The compositions of the present invention in some alternative aspects of the invention can include supplemental solubilizing agents such as propylene glycol in amounts from about 5 to about 30% v/v. In these alternative aspects, the amount of ethanol in the ready to dilute composition would be at least about 70% v/v or about 80% v/v. One suitable solvent system in accordance with this aspect of the invention provides cyclophosphamide compositions which contain about 70% ethanol, about 30% propylene glycol, and about 0.5% thioglycerol.

Palepu at [0019].

45. Palepu teaches that the solubility of cyclophosphamide monohydrate was in excess of 500 mg/ml in propylene glycol, polyethylene glycol, and ethanol, which is beneficial as the solution can be safely diluted for intravenous administration:

> In this example, studies were initiated to determine the solubility of cyclophosphamide monohydrate in pharmaceutically acceptable solvents such as propylene glycol, polyethylene glycol and ethanol. It was surprisingly found that the solubility of cyclophosphamide monohydrate was in excess of 500 mg/ml in each of these solvents. The advantage of making a 500 mg/ml solution is that when diluted to achieve the desired 20 mg/ml solution of cyclophosphamide, suitable for intravenous administration, the organic solvent concentration in the admixture is less than about 3% which is a safe level to administer intravenously.

Palepu at [0033].

46. However, Palepu further discovered that "data obtained from studies in pure solvents… was not satisfactory" and "[s]ignificant degradation was observed when PG and PEG 400 were used as sole solvents." Palepu at [0035]. Palepu taught that "the stability of cyclophosphamide in ethanol appeared to be significantly better compared to the other two solvents." Palepu at [0035], Table 5.

47. Palepu then describes the degradation chemistry of cyclophosphamide and studied "the effects of small quantities of anhydrous citric acid" as well as calcium chloride dihydrate to slightly acidify the solution and avoid degradation reactions, improving stability:

HIGHLY CONFIDENTIAL –
SUBJECT TO PROTECTIVE ORDER

TABLE 6

Stability of Cyclophosphamide (CPP) in Ethanol Containing Citric Acid and Calcium Chloride

Excipient	Storage T° C.	Storage Period(M)	CPP Content (mg/mL)	% of Initial
Citric acid		Initial	451.9	100.0
2 mg/ml	25	1	448.6	99.1
		3	430.6	95.3
	15	6	437.9	96.9
	5	6	440.0	97.4
		18	451.6	99.9
Citric acid		Initial	425.3	100.0
4 mg/ml	25	1	432.7	101.7
		3	413.8	97.3
	15	6	419.0	98.5
	5	6	420.0	98.8
		18	433.7	102.0
Citric acid		Initial	453.2	100.0
6 mg/ml	25	1	459.6	101.4
		3	431.4	95.2
	15	6	445.0	98.2
	5	6	446.0	98.4
		18	448.0	98.9
Citric acid		Initial	492.1	100.0
8 mg/ml	25	1	491.0	99.8
		3	461.0	93.7
	15	6	467.9	95.1
	5	6	489.6	99.5
		18	NA	NA
Citric acid		Initial	494.2	100.0
10 mg/ml	25	1	493.6	99.9
		3	465.0	94.1
	15	6	465.3	94.2
	5	6	488.9	98.9
		18	473.3	95.8
Calcium		Initial	550.7	100
Chloride	25	1	551.1	100.1
Dihydrate		3	523.9	95.0
2 mg/ml	15	6	542.5	98.5
	5	6	545.0	99.0
		18	545.8	99.1

Palepu at [0037], Table 6.

48. Additionally, Palepu discloses the inclusion of antioxidants into its formulation:

> The pharmaceutically acceptable cyclophosphamide containing solutions can also include an anti-oxidizing agent such as, for example, thioglycerol, propyl gallate, methionine, cysteine and combinations thereof. Thioglycerol is a preferred antioxidant. Useful concentrations of the antioxidant in the inventive compositions can be [sic] range from about 1 to about 8 mg/ml.

Palepu at [0017].

4. Shaik (2016)

49. International Publication No. WO 2016/005962 ("Shaik", DTX-006) is prior art to the asserted patents under either 35 U.S.C. § 102(a)(1) because it was published January 14, 2016, prior to the filing date of February 15, 2016.

50. In short, Shaik teaches forming stable liquid cyclophosphamide formulations using ethanol as a solvent and dehydrating the cyclophosphamide to remove the waters of hydration, avoiding the hydrolysis reactions that form the known impurities A-D.

51. Shaik teaches forming cyclophosphamide formulations "comprising a step of reducing the moisture content from cyclophosphamide." Shaik at Abstract, 13 ("It was understood that probably the bound water of cyclophosphamide monohydrate (approximately 6.25 %) may be responsible for hydrolytic degradation cyclophosphamide in anhydrous ethanol."). For example, Shaik teaches reducing moisture content by "selecting a suitable drying process selected from the group comprising vacuum drying, lyophilization, solvent evaporation." Shaik at 6-7.

52. Shaik investigates examples using pure ethanol with reduced water content cyclophosphamide:

Example 1: Pharmaceutical formulation of cyclophosphamide with reduced water content by vacuum drying

Ingredients	Quantity
Cyclophosphamide monohydrate*	500mg
Anhydrous ethanol	Qs to 1mL

Shaik at 28-29.

53. Shaik teaches that this formulation exhibits excellent stability:

Table 1

Stability condition	Time period	Description	Total impurities (%)
	Initial	Clear solution	0.06
25ºC	1 week	Clear solution	0.20
	2 week	Clear solution	0.54
	1 month	Clear solution	0.97
	3 months	Clear solution	2.8
40ºC	1 week	Clear solution	0.84
	2 week	Clear solution	3.82

Shaik at 29-30. For context, at 1 week at 40° C, Shaik's formulations exhibit 0.84% total impurities, compared to 1.87, 2.01, and 2.33 for the examples of the 952 patent. *See* 952 Patent at Table 1.

54. Shaik also provides other examples of forming ethanolic solutions using PEG or PG. *E.g.*, Examples 9 and 10.

Example 11-14: Pharmaceutical liquid formulations of cyclophosphamide.

Ingredients	Example 11	Example 12	Example 13	Example 14
		Quantity/mL		
Cyclophosphamide	500 mg	500 mg	500mg	500mg
Polyethylene glycol (PEG300)	0.1mL to 0.9mL	-	-	-
Propylene glycol	-	0.1mL to 0.9mL	-	-
Polysorbate 80	-	-	0.1mL to 0.9mL	-
Cremophor EL	-	-	-	0.1mL to 0.9mL
Anhydrous Ethanol	Qs to 1mL	Qs to 1mL	Qs to 1mL	Qs to 1mL

Shaik at 37-38*; see also* Shaik at 8 ("In one of the embodiment the invention includes stable liquid formulations of cyclophosphamide wherein the suitable solvent selected from the group comprising of alcohol, polyethylene glycol, propylene glycol, dimethyl acetamide, glycerol, polysorbate 80, polyethoxylated castor oil or combinations thereof.").

5. Tait (2002)

55. International Publication No. WO 02/02125 ("Tait", DTX-010) is prior art to the asserted patents under 35 U.S.C. § 102(a)(1) because it was published in 2002, prior to the earliest possible priority date for the asserted patents of February 16, 2015.

56. In short, Tait teaches forming stable formulations of a related compound, ifosfamide, using ethanol with a co-solvent to reduce handling issues with purely ethanolic solutions.

57. Tait teaches the advantages of a solvent mixture comprising ethanol and higher boiling polyols, such as polyethylene glycol, and propylene glycol for use with ifosfamide (a compound closely related to cyclophosphamide). See, e.g., Tait at 16:27-29 ("It will be appreciated

that the compositions of the invention provide significant advantages in the transport, storage and handling of ifosfamide injectable compositions for use in treatment of tumours.”).

58. Tait further teaches that “in a first aspect of the invention there is provided a liquid pharmaceutical composition for parenteral administration comprising ifosfamide, solvent and optionally, conventional pharmaceutical carriers and excipients, wherein said solvent comprises 35-75% lower alcohol (based on the total weight of the solvent) and 25-65% polyol (based on the total weight of the solvent).” Tait at 4:25-29. Tait teaches that these formulations are “chemically stable to hydrolysis” and can avoid the need for reconstitution. Tait at 4:30-5:8.

59. Tait teaches that “[d]esirably, the composition is substantially anhydrous” because it “should be recalled [] that since the oxazaphosphorins are susceptible to hydrolysis, degradation may be minimized by limiting the presence of water.” Tait at 6:30-7:4.

60. Tait provides numerous examples exhibiting good stability with ifosfamide, summarized below:

Example	1	2	3	4	5
Ethanol	35%	75%	75%	35%	75%
PEG 400	65%	25%			
Glycerol			25%		
Propylene Glycol				65%	25%
Concentration	10.27 mg/g	11.42 mg/g	11.28 mg/g	11.23 mg/g	12.23 mg/g
Ifosfamide remaining after 1 month at 4°C	100%	100%	100%	99.4%	99.3%
Ifosfamide remaining after 1 month at 50°C	94.7%	97.9%	97.0%	96.3%	98.0%

61. While a POSA would understand that Tait is using ifosfamide – not cyclophosphamide and thus the results of the testing cannot be directly compared to formulations using cyclophosphamide, a POSA would nevertheless understand that Tait’s teachings of the relative performance of different formulations can be applicable to cyclophosphamide—i.e., that utilizing relatively higher amounts of ethanol with relatively smaller amounts of PEG and/or PG

would likely increase stability while maintaining handling. *See, e.g.*, Tait at 1:178-19 ("Ifosfamide, a synthetic analogue of cyclophosphamide…."); Sauerbier at 3:46-48 ("Especially suitable oxazaphosphorins for the present invention and those of therapeutic importance, are cyclophosphamide and ifosfamide.").

B. Differences between the prior art and the claims and level of skill in the art

62. The prior art does not provide a specific example of a formulation falling within the scope of the claims. However, as described above the prior art teaches that each of the claimed ingredients is useful in forming stable formulations and that relatively high amounts of ethanol with relatively lower amounts of PEG and/or PG increased stability. Thus, it would have taken only routine experimentation to vary the ratios of the different solvents to achieve stable formulations with an optimal concentrations of cyclophosphamide.

63. A POSA would have been motivated to engage in such routine experimentation in order to improve the stability of the resulting formulations while maintaining safe handling.

64. A POSA would have understood that cyclophosphamide formulations should be concentrated to avoid the need for excessive dilution, but that too high a concentration could cause precipitation or impurities formed by self-alkylation degradation. Thus, a POSA would have been motivated to investigate formulations encompassing a range of 12-23% cyclophosphamide. Further, there is nothing critical about this range – stable formulations could be made (and were made in the prior art) with higher and lower levels of cyclophosphamide.

65. A POSA would have understood that ethanol would be the preferred primary solvent for maximizing stability. For example, Palepu, Shaik, Tait and Sauerbier all demonstrate the effectiveness of ethanolic solvent systems. Thus, a POSA would have been motivated to investigate formulations encompassing a range of 70-75% ethanol. Further, there is nothing critical

about this range – stable formulations could be made (and were made in the prior art) with higher and lower levels of ethanol (especially higher). For example, the inventors' own testing and submitted declarations demonstrate that compositions with higher ethanol concentrations were actually more effective in increasing stability:

Table 4: Stability details of Instant Application with varying ratios of PEG and PG (1:1, 1:2, 2:1) with and without MTG.

1 week at 40°C 75%RH									
PG:PEG	1:1 ratio			1:2 ratio			2:1 ratio		
PG:PEG :Ethanol	1.25:1.25: 97.5	5:5: 90	12.5:12.5: 75	0.83:1.67: 97.5	3.33:6.67: 90	8.33:16.67: 75	1.67:0.83: 97.5	6.67:3.33: 90	16.67:8.33: 75
Without MTG									
Assay-initial	100.1	100.8	101.7	104.2	101.4	98.2	102.1	102.9	99.8
Assay- 1week*	98.7	98.2	98.2	101.6	99. 2	96	100 .1	99 5	97 .7
Tota limpu rities	2.77	2.93	3. 56	3 .3 8	3. 13	3. 4	22.8 3	3.18	3 .32
Drop in assay	1.4	2.6	3.5	2.6	2.2	2.2	2.0	3.4	2.1
With MTG									
Assay-initial	99.6	100.4	98.1	100.2	99.1	98.6	100.5	100.0	98.6
Assay- 1week*	97.8	97.1	95.1	97.2	97.3	95.3	97.5	96.6	95.1
Total impurities	3.48	3.55	3.86	2.65	3.13	3.42	2.95	3.43	3.91
Drop in assay	1.8	3.3	3.0	3.0	1.8	3.3	3.0	3.4	3.5

See DTX-002 at 148. Shaik further achieved even lower levels of impurities after 1 week at 40°C using pure ethanol.

66. A POSA would have understood it would have been advantageous to use PEG and PG as cosolvents/solubilizing agents. Tait teaches that such solvents maintain solubility and stability while avoiding some of the handling issues of pure ethanol. Alam teaches that PEG and PG cosolvents provide good stability in combination. Palepu and Shaik both teach that PEG and PG can be use as cosolvents. Thus, a POSA would have been motivated to investigate formulations encompassing 3.4-8.8% PEG and 3.4-4.4% PG. Further, there is nothing critical about the claimed ranges or the use of both PEG and PG–stable formulations could be made (and were made in the prior art) with higher and lower levels of PEG or PG or using one or the other.

67. The prior art further taught the use of antioxidants, including monothioglycerol, to avoid oxidation reactions and improve stability. For example, Palepu teaches "The pharmaceutically acceptable cyclophosphamide containing solutions can also include an anti-oxidizing agent such as, for example, thioglycerol…." Palepu at [0017]. Shaik similarly states "Additional excipients that can be included in the liquid formulations of the present invention include antioxidants" and that "[s]uitable antioxidants include but not limited to …. monothiogleycerol." Shaik at 23. Shaik further teaches using such antioxidants "at a range of about 0.01 % w/w to about 10% w/w of the formulation." *Id.* Thus, it would have been obvious to use an antixodiant, including monothioglycerol, at concentrations of 0.01% to about 0.02%. Further, there is nothing critical about this range – stable formulations could be made (and were made in the prior art) without antioxidants, with other antioxidants, or at higher and lower levels of monothioglycerol.

68. A stable formulations with ethanol, PEG, and PG (and monothioglycerol) would have taken only routine experimentation—modify the formulation and test it for stability—which would have been well within the skill of a POSA.

69. Thus, a POSA would have had a reasonable expectation of success in developing stable formulations (meeting the claim limitations) by optimizing the various concentrations of the solvent system, removing water, and using stabilizing agents such as monothiol glycerol, citric acid, and calcium chloride. For example, the inventors' own testing showed Palepu's (unoptimized) example formulation met two of the three impurity limitations (A and B) and impurity D was low (<1%), and only slightly higher than the limitation (0.79% v. 0.5%). The same is true of Alam Formulation 11, which was only slightly higher than the limit in impurity B. It would have been very routine in the art to optimize the prior art and achieve improved results.

C. Objective indicia

1. Alleged unexpected results

70. The claims were allowed because the inventors submitted declarations alleging unexpected results of the claimed formulations compared to specific examples of Palepu and Alam. However, the inventors' data does not suggest unexpected results or non-obviousness, and at best the results show a modest improvement over the explicit examples of Alam and Palepu. In other words, it is at best a difference in degree, not in kind. For example, the inventor's declaration shows only a modest improvement over Palepu and Alam's disclosed formulations:

Parameter	Ex-02		90:5:5 (EtOH:PEG400:PG)		Palepu	
	Initial	1Week 40°C	initial	1 week 40° c	Initial	1Week 40°C
%assay	101.6	101.9	100.4	97.1	102.4	95.8
%ImpA	ND	ND	0.02	0.05	ND	0.33
%ImpB	0.06	0.18	0.04	0.22	0.06	0.23
%ImpD	ND	ND	0.02	0.12	0.01	0.79
%Total imp	0.07	1.87	0.08	3.55	0.11	*7.29
	Increase in impurities to 1.87%		Only 3.3% drop in assay Increase in total impurities to 3.55%		6.6% assay difference Increase in total impurities to 7.29%	

Note: Total impurities is the sum of imp A, imp B, imp C and other impurities.

DTX-002 at ING00000086. Palepu meets the claimed limits of 0.5% for impurities A and B and only narrowly misses for impurity D.

Comparison with Alam (data except assay values of Alam formulation are part of Oct 2019 declaration)

	EX-02		90:5:5		Alam formulations					
					Formulation 1		Formulation 7		Formulation 11	
Parameter	Initial	1Week 40°C	initial	1 week 40 °C	Initial	1WK 40°C	Initial	1WK 40°C	Initial	1WK 40°C
%assay	101.6	101.9	100.4	97.1	94.8	56.2	100.8	41.2	93.8	87
%ImpA	ND	ND	0.02	0.05	ND	2.74	0.03	2.98	ND	ND
%ImpB	0.06	0.18	0.04	0.22	0.54	ND	0.98	0.95	0.12	0.74
%ImpD	ND	ND	0.02	0.12	ND	ND	ND	39.48	ND	ND
%Total imp	0.07	1.87	0.08	3.55						

DTX-002 at ING0000089. Similarly, Alam's formulation 11 has no formation of impurities A and D and only narrowly exceeds the claimed 0.5% limit for impurity B.

71. At best, the presented data seems to show that the inventors were able to slightly improve stability over Palepu and Alam.

72. Notably, the comparisons above compare apples and oranges. The Palepu formulations are much more concentrated (550 mg/ml) which may account for the different stability. For example, when Palepu was commercialized, it was commercialized at a much lower concentration (500 mg / 2.5 ml), a teaching which is in Palepu. Further, the testing does not account for Palepu's teaching of using monothioglycerol, which may also account for the differences, or the teachings in the art of using PEG and PG.

73. Further, the results were not compared to Shaik, which achives total impurities 0.84% after 1 week at 40 °C, better than any of the tested formulations.

2. Alleged long-felt need

74. While there was a need for stable liquid formulations in the art, this need was offset to some degree by the fact that cyclophosphamide was already available as a lyophilized powder.

75. Further, the need for stable formulations was already met by the teachings of Palepu and Shaik.

VI. FACTS RELATED TO LACK OF WRITTEN DESCRIPTION AND ENABLEMENT UNDER 112

76. Each of the asserted claims are directed to "[a] stable liquid parenteral formulation of cyclophosphamide." Claim 1 further requires that decomposition to form certain impurities is less than 0.5% for each of the claimed impurities. The specification does not teach that the inventors were in possession of the full scope of the claimed invention. Further, to the extent Plaintiff argues undue experimentation was necessary to achieve the claimed invention despite the detailed teachings of the prior art (i.e., that a POSA would not have had a reasonable expectation of success), the same experimentation would have been required to achieve the full scope of the claims here following the teachings of the 952 patent (testing various formulations with differing amounts of ethanol, PEG, and PG), and thus the specification would not enable the claims.

77. Of the eight example formulations included in the specification, the 952 patent includes stability data with respect to the claimed impurities for only three of these example formulations. See Table 1 (including stability data for Examples 2, 4, and 5). However, the compositions of Examples 4 and 5 clearly fall outside the scope of every claim of the 952 patent. For example, neither Example 4 nor Example 5 includes propylene glycol, which is required by every claim of the 952 patent.

78. Example 2 – the only disclosure in the 952 patent of stability data for a formulation encompassed by any of the claims – includes 1.0 g cyclophosphamide, 0.733 g PEG 400, 6.23 g

ethanol, 0.367 g propylene glycol, and 0.69 mg monothioglycerol. This equates to 12.00% cyclophosphamide, 8.80% PEG 400, 74.78% ethanol, 4.41% propylene glycol, and 0.0083% monothioglycerol based on total formulation weight.

79. This single example fails to demonstrate to a POSA that the inventors were in possession of the claimed stable formulations (i.e., formulations with about 12-23% cyclophosphamide, about 70-75% ethanol, etc.) that all fell within the claimed purity requirements. Indeed, the specification suggests the inventors had tested a single formulation within the scope of the claims and were unsure of whether other formulations would be similarly successful.

80. Many embodiments falling within the claimed ranges are impossible (e.g. because the claim 1 formulation requires at least about 3.4% PG and 3.4% PEG, (6.8% total), formulations with 23% cyclophosphamide could have a maximum of 70.2% ethanol. Much of claim 4 is similarly impossible – as the claim requires 23% cyclophosphamide, and 70% ethanol, which account for 93% of the total weight. Thus, the PEG and PG combined can only total 7% and must be approximately 3.5% each (making the claimed scopes of 3.4-8.8% or 3.4-4.4% meaningless).

EXHIBIT 4

UNREDACTED PUBLIC VERSION

EXHIBIT 4

PLAINTIFFS' STATEMENT OF ISSUES OF LAW THAT REMAIN TO BE LITIGATED

Pursuant to D. Del. LR 16.3(c)(5), Plaintiffs submit the following statement of issues of law which remain to be litigated,. The following statements are meant to serve as an overview of the contested issues of law to be litigated at trial. Plaintiffs reserve the right to prove any matters identified in its pleadings, discovery responses, including in its contentions, and/or expert reports and depositions, and to rebut evidence offered by Defendant. Plaintiffs reserve the right to modify or amend this Exhibit to the extent necessary to reflect any future rulings by the Court, and to supplement or amend this Exhibit to fairly respond to any new issues that Defendants may raise.

To the extent Plaintiffs' statement of contested facts, which is submitted as Exhibit 2 hereto, contains issues of law, those issues are incorporated herein by reference. Likewise, if any issue of law identified below should properly be considered an issue of fact, then such statement should be considered to be part of Plaintiffs' statement of contested facts. The authority cited by Plaintiffs is exemplary. Plaintiffs may rely on additional or different authority in its trial brief, post-trial submissions, or any other presentation to the Court. Plaintiffs reserve the right to respond to and contest any issue raised by Defendant.

TABLE OF CONTENTS

I. PERSON OF ORDINARY SKILL IN THE ART 4

II. INFRINGEMENT 5

A. CLAIM CONSTRUCTION 6

B. INFRINGEMENT 9

1. Direct Infringement under § 271(e)(2)(A) 10

2. Direct Infringement under § 271(a) 10

3. Indirect Infringement 11

III. VALIDITY 14

A. ACCORD HAS NOT SHOWN BY CLEAR AND CONVINCING EVIDENCE THAT THE CLAIMS OF THE ’952 PATENT ARE OBVIOUS 15

1. Objective Indicia of Nonobviousness 24

2. Issues of Law Relating to Obviousness 30

B. ACCORD CANNOT ESTABLISH BY CLEAR AND CONVINCING EVIDENCE THAT THE ’952 PATENT SPECIFICATION FAILS TO DEMONSTRATE THAT THE INVENTOR POSSESSED THE INVENTION 33

1. Issues of Law Relating to Written Description 35

C. ACCORD CANNOT ESTABLISH BY CLEAR AND CONVINCING EVIDENCE THAT THE ’952 PATENT FAILS TO TEACH A PERSON OF ORDINARY SKILL HOW TO MAKE AND USE THE INVENTION 36

1. Issues of Law Relating to Enablement 39

D. ACCORD CANNOT ESTABLISH THAT CLAIMS 1-4 OF THE ’952 PATENT FAIL TO INFORM A PERSON OF ORDINARY SKILL IN THE ART ABOUT THE SCOPE OF THE CLAIMS 40

1. Issues of Law Relating to Indefiniteness 40

E. PLAINTIFFS ARE ENTITLED TO AN INJUNCTION PRECLUDING ACCORD FROM SELLING ITS GENERIC CYCLOPHOSPHAMIDE PRODUCTS BEFORE THE ’952 PATENT-IN-SUIT EXPIRES 41

IV. THIS IS AN EXCEPTIONAL CASE 42

I. PERSON OF ORDINARY SKILL IN THE ART

1. Plaintiffs contend that a person of ordinary skill in the art or a "POSA" "is deemed to read the words used in the patent documents with an understanding of their meaning in the field, and to have knowledge of any special meaning and usage in the field. The inventor's words that are used to describe the invention—the inventor's lexicography—must be understood and interpreted by the court as they would be understood and interpreted by a person in that field of technology." *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477 (Fed. Cir. 1998).

2. The person of skill "is presumed to be aware of all the pertinent art. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 448 (Fed. Cir. 1986); *see also Senju Pharm. Co. v. Apotex Inc.*, 717 F. Supp. 2d 404, 422 (D. Del. 2010), *aff'd*, 485 F. App'x 433 (Fed.Cir. 2012) ("[O]ne of ordinary skill is presumed to have knowledge of all pertinent prior art-be it obscure [o]r unknown to actual individual."); *Daiichi Sankyo Co. v. Mylan Pharm. Inc.*, 670 F. Supp. 2d 359, 370 (D.N.J. 2009), *aff'd sub nom. Daiichi Sankyo Co. v. Matrix Labs., Ltd.*, 619 F.3d 1346 (Fed. Cir. 2010) ("Under the standard for obviousness, a person of ordinary skill is presumed to have knowledge of all prior art references.") (citing *In re Gorman*, 933 F.2d 982, 986 (Fed. Cir. 1991)).

3. Factors that may be considered in determining the ordinary level of skill in the art include, at least, "1) the types of problems encountered in the art; 2) the prior art solutions to those problems; 3) the rapidity with which innovations are made; 4) the sophistication of the technology; and 5) the educational level of active workers in the field."*Ruiz v. A.B. Chance Co.*, 234 F.3d 654, 666–67 (Fed. Cir. 2000); *see also Environmental Designs, Ltd. V. Union Oil Co.*, 713 F.2d 693, 696–97 (Fed. Cir. 1983).

4. The specification guides the determination of the appropriate level of skill in the art. *See, e.g.*, *Hologic, Inc. v. Minerva Surgical, Inc.*, 2019 WL 1760167 (Fed. Cir. 2019) ("While the claims are directed to uterine ablation, the patent specification speaks in terms of 'body cavities, with the uterus comprising just one example."); *Mintz v. Dietz & Watson, Inc.*, 679 F.3d 1372 (Fed. Cir. 2012) (The . . . specification repeatedly focuses on the meat encasement art. . . . Accordingly, the level of ordinary skill in the art of the claimed invention includes the meat encasement art").

II. INFRINGEMENT

5. It is an act of infringement to file an Abbreviated New Drug Application ("ANDA") seeking approval to use a drug in a manner claimed by a patent. See 35 U.S.C. § 71(e)(2)(A) ("It shall be an act of infringement to submit an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act . . . for a drug claimed in a patent or the use of[,] which is claimed in a patent, . . . if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug, veterinary biological product, or biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.") (emphasis added).

6. A patent owner must prove infringement by a preponderance of the evidence, which requires only that it is more likely than not that infringement will occur. *See SmithKline Diagnostics, Inc. v. Helena Labs. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988).

7. To prove direct infringement, "a patentee must show that an accused product or method meets every claim limitation either literally or under the doctrine of equivalents." *Pfizer, Inc. v. Teva Pharms., USA, Inc.*, 429 F.3d 1364, 1376 (Fed. Cir. 2005). "A patentee may prove

direct infringement . . . by either direct or circumstantial evidence." *Liquid Dynamics Corp. v. Vaughan Co.*, 449 F.3d 1209, 1219 (Fed. Cir. 2006).

8. The infringement analysis will require determining the meaning and scope of the patent claims and then comparing the properly construed claims to the allegedly infringing device or process in order to determine whether the accused product falls within the scope of the properly construed claims. See *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), aff'd, 517 U.S. 370 (1996). In construing a claim, the words of the claim are generally given their ordinary and customary meaning. *Phillips v. AWH Corp*., 415 F.3d 1303, 1312 (Fed. Cir. 2005). The ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application. *Id*. at 1313.

A. CLAIM CONSTRUCTION

9. Defendant contended during claim construction that the following terms are indefinite (D.I. 34 and 34-1): (1) Claim 1 -- "an ethanol content of about 70% to about 75% based on total formulation weight" and "cyclophosphamide in a concentration of about 12% to about 23%"; and (2) Claim 4 -- "an ethanol content of about 70% based on total formulation weight."

10. Defendant alternatively contended that the term "an ethanol content of about 70% to about 75% based on total formulation weight" (Claim 1) and "an ethanol content of about 70% based on total formulation weight" (Claim 4) should be construed as "an ethanol content of 70% to 75% based on total formulation weight" (Claim 1) and "an ethanol content of 70% based on total formulation weight" (Claim 4). D.I. 34 and 34-1

11. Plaintiff contends that Claims 1-4 of the '952 Patent are not indefinite and the term "about" should be construed as "approximately." D.I. 34 and 34-1. Plaintiff advised the Court that

the term "about" recited in claims 1-4 of the '952 Patent has recently been construed in this manner in a related case. D.I. 54.

12. The Motions for Claim Construction filed by Plaintiffs and Defendant (D.I. 35 and 36) were denied. D.I. 37. The Court indicated that it "will hear the indefiniteness defense(s) at the bench trial" and the scheduled Markman hearing was cancelled. *Id.*

13. The term "about" provides some scope of claim coverage beyond the strict numerical end points recited. The Federal Circuit in *Cohesive Technologies, Inc. v. Waters Corp.*, 543 F.3d 1351, 1368 (Fed. Cir. 2008) stated that "[t]he word 'about' does not have a universal meaning in patent claims, and [its] meaning depends on the technological facts of the particular case." *Id.*

14. Claims are interpreted by reference to the intrinsic evidence, including the claims, the specification and the prosecution history. *Phillips v. AWH Corp*., 415 F.3d 1303, 1315 (Fed. Cir. 2005 (*en banc*)), citing *Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996).* The claims recite "about 70% to about 75%" ethanol and "about 23%" cyclophosphamide. The term "about" appears not less than 16 times in the claims. Because it is legally presumed that that the same terms appearing in different portions of the claims should be given the same meaning, *see e.g., Phillips*, 415 F.3d at 1314; *Rexnord Corp. v. Laitram Corp*., 274 F.3d 1336, 1342 (Fed. Cir. 2001), the repeated use of "about" in other claims (referring to other formulation amounts) informs the construction of "about" in Claim 1.

15. The specification, states that "[t]he quantity of solvents ranges from about 40-99% by weight of the composition" (Col. 3, ll. 29-31), and that a preferred embodiment has as a solvent ethanol (20-98%), and a most preferred embodiment has as a solvent ethanol (40-92%). Col. 3, ll. 49-67. The Examples disclose ethanol amounts (based on total formulation weight) of 74.81%

(Ex. 2), 70.58% (Ex. 6) and 70.12% (Ex.8). The specification therefore provides guidance regarding how far a person skilled in the art could extend the terms "about 70%" and "about 75%" because it does provide boundaries. *Phillips* 415 F.3d at 1315 (Claims are interpreted by reference to the intrinsic evidence, including the claims, the specification and the prosecution history.)

16. During prosecution, the Examiner stated that a comparative example containing 69.81% ethanol was encompassed by the claims and that examples containing 23.25%, 22.62%, 22.52% cyclophosphamide could be considered as approximately 23% as claimed. *Phillips* 415 F.3d at 1317 ("the prosecution history provides evidence of how the PTO and the inventor understood the patent.")

17. Courts have construed "about" in reference to an amount or a range as meaning "approximately." *Kim v. Dawn Food Products, Inc*., 2004 U.S. Dist. LEXIS 20837, *15-16 (N.D. Ill., Oct. 12, 2004)(construing "about 0.001 to 0.03 parts ascorbic acid" to mean "approximately 0.001 to 0.03 parts ascorbic acid"); *Novartis Pharm. Corp. v. Apotex Corp*., 2006 U.S. Dist. LEXIS 10130, *29 (S.D.N.Y. Mar. 13, 2006)("The plain and ordinary meaning of 'about,' and how it would be read by one skilled in the art, is 'approximately'"); *Chiron Corp. v. Sourcecf Inc., et al*., 2005 U.S. Dist. LEXIS 34450, *11 (N.D. Cal., Dec. 1, 2005) ("about 60 to about 200 mg/ml" construed to mean "approximately 60 to approximately 200 mg/ml"); *Biopolymer Engineering, Inc., et al. v. Immunocorp, et al*., 2007 U.S. Dist. LEXIS 94207, *44 (D. Minn., Dec. 21, 2007) (construing "about 0.20 mg to about 1.0 mg of said supplement" as "approximately 0.20 mg to approximately 1.0 mg of said supplement").

18. The Federal Circuit has recognized that use of a term such as "about" avoids a "strict numerical boundary to the specified parameter" and that the range "must be interpreted in its technological and stylistic context." *Central Admixture Pharmacy Servs., Inc. v. Advanced*

Cardiac Solutions, P.C., 482 F.3d 1347, 1355-56 (Fed. Cir.), *cert. den.* 128 S. Ct. 648 (2007); *Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd.*, 476 F.3d 1321, 1326-28 (Fed. Cir. 2007); *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1217-18 (Fed. Cir. 1995).

19. In a related case, *Ingenus Pharms., Inc. et al. v. Nexus Pharms., Inc.*, No. 22-cv-2868 (N.D. Il July 31, 2024), the Court rejected challenge to the "about" terms in Claims 1-4 of the '952 Patent as indefinite, and construed "about" in the '952 Patent claims to mean "approximately." D.I. 54-1, Ex. A. The Court relied on the patent specification and prosecution history, citing the patent examiner's statement that "the upper limit of cyclophosphamide of the specific examples of the patent is 23.25%, 22.62%, 22.52%, which could be interpreted as approximately 23%," the Court concluded that "[t]he examiner understood "about" to mean approximately and understood amounts of cyclophosphamide above 23% to be included within a claim reciting 23% as a numerical endpoint." *Id.*

B. INFRINGEMENT

20. Plaintiffs contend that the following issues of law relating to infringement remain to be litigated:

i. whether Defendants directly infringes the '952 Patent under 35 U.S.C. § 271(e) based on Defendant's ANDA 218250;

ii. whether Defendants directly infringe claims 1-4 of the '952 Patent pursuant to 35 U.S.C. § 271(a); and

iii. whether Defendants indirectly infringe claims 1-4 by inducing direct infringement under 35 U.S.C. § 271(b) and contributing to the direct infringement of claims 1-4 of the '952 Patent pursuant to 35 U.S.C. § 271(c).

1. Direct Infringement under § 271(e)(2)(A)

21. Plaintiffs contend that the submission and filing of Defendant's ANDA with a Paragraph IV certification to the '952 Patent was an act of direct infringement by Defendant under 35 U.S.C. § 271(e)(2)(A). Additionally, Plaintiffs contend that the manufacture, use, offer for sale, sale and/or importation of the Accused Products within the United States by Defendant directly infringes, or will directly infringe, the asserted claims of the '952 Patent under 35 U.S.C. § 271(a).

22. Plaintiffs also contend that Defendant's ANDA seeks approval from the FDA for ranges of amounts of cyclophosphamide and ethanol that if approved would constitute infringement of the '952 Patent because "[w]hat a generic asks for and receives approval to market, if within the scope of a valid claim, is an infringement." *Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.*, 731 F.3d 1271, 1279 (Fed. Cir. 2013); *id.* at 1278 ("[I]f a product that an ANDA applicant is asking the FDA to approve for sale falls within the scope of an issued patent, a judgment of infringement must necessarily ensue.").

2. Direct Infringement under § 271(a)

23. Defendant's ANDA Products directly infringe claims 1-4 of the '952 Patent pursuant to 35 U.S.C. § 271(a).

24. Plaintiffs contend that the Defendant's ANDA Products include all the elements of Claims 1-4 of the '952 Patent, and therefore literally and directly infringe these claims.

25. If Defendant's ANDA Products do not literally infringe, Plaintiffs further contend that they infringe claims 1-4 of the '952 Patent under the doctrine of equivalents. Plaintiffs contend that Defendant's ANDA Products contain each ingredient recited in claims 1-4 of the '952 Patent in an amount that performs substantially the same function in substantially the same way to achieve

the same result as the claimed element, and/or are insubstantially different from the claimed ingredient.

3. Indirect Infringement

26. Defendant's ANDA Products indirectly infringe claims 1-4 by inducing direct infringement under 35 U.S.C. § 271(b) and contributing to the direct infringement of claims 1-4 of the '952 Patent pursuant to 35 U.S.C. § 271(c), based on Defendant's intention to sell, offer to sell, or import into the United States components for use in infringing products.

27. Plaintiffs contend that Defendant is liable for induced infringement because it: (a) knew of the '952 Patent since 2021, (b) has or intends to encourage others (like patients, pharmacists, hospitals and doctors) to directly infringe the '952 Patent, and (c) others (like patients, pharmacists, hospitals and doctors)) will actually use the products as encouraged and/or directed by Defendant. 35 U.S.C. § 271(b); *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010); *see also Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc.*, 843 F.3d 1315, 1332 (Fed. Cir. 2016).

a. Induced Infringement

28. To prove induced infringement, the patentee must show direct infringement, and that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another's infringement. *Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1363 (Fed. Cir. 2012); *see also AstraZeneca*, 633 F.3d at 1056 (internal quotation marks omitted). However, as with direct infringement, "direct evidence is not required; rather, circumstantial evidence may suffice" to establish induced infringement. *AstraZeneca*, 633 F.3d at 1060; *see also Liquid Dynamics*, 449 F.3d at 1219.

29. In Hatch-Waxman cases, drug labels routinely constitute conclusive proof of specific intent to infringe. *See, e.g.*, *Eli Lilly*, 435 F. App'x at 926; *AstraZeneca*, 633 F.3d at 1059–60; AstraZeneca *LP v. Breath Ltd.*, 2013 WL 1385224, at *9 (D.N.J. Apr. 3, 2013). If a drug label instructions "will cause at least some users" to engage in an infringing use, the trial court may "infer from [such] instructions an affirmative intent to infringe the patent." *AstraZeneca*, 633 F.3d at 1059–60; *see also Sanofi v. Glenmark Pharm. Inc., USA*, CV-14-264-RGA, 2016 WL 4569680, at *3 (D. Del. Aug. 31, 2016) ("In Hatch-Waxman cases alleging that a proposed drug label will induce infringement by physicians, 'The pertinent question is whether the proposed label instructs users to perform the patented method.'") (quoting *AstraZeneca*, 633 F.3d at 1060).

30. A label need not use magic words, to support an inference of specific intent. See *In re Omeprazole Patent Litig*., 258 F. Supp. 2d 221, 234–35 (S.D.N.Y. 2001) (the "absence of direct instruction on infringement to customers . . . does not foreclose [a] finding of active inducement"). The label need only support an inference of specific intent to infringe. *See, e.g., L.A. Biomedical Res. Institute v. Eli Lilly & Co*., 2014 WL 11241786, at *3–6 (C.D. Cal. May 12, 2014); *Bone Care Int'l, L.L.C. v. Roxane Labs., Inc*., 2012 WL 2126896, at *4, 8, 11–12 (D. Del. June 11, 2012).

31. "Even [t]he existence of a substantial non-infringing use does not preclude" a finding of specific intent to induce infringement. *Toshiba Corp. v. Imation Corp*., 681 F.3d 1358, 1364 (Fed. Cir. 2012); *see also Breath*, 2013 WL 1385224, at *9 (quoting *Toshiba*, 681 F.3d at 1364).

32. A defendant's belief regarding patent validity is not a defense to a claim of induced infringement. *Commil USA, LLC v. Cisco Sys., Inc*., 2015 U.S. LEXIS, at *16 (S. Ct. May 26, 2015).

33. Defendant will actively encourage the use of its ANDA Products by others, *e.g.*, patients, pharmacists, hospitals and physicians, after it had knowledge of the ’952 Patent, and Defendant knew or should have known that its active encouragement and promotion would result in infringement of the ’952 Patent. *DSU Med. Corp. v. JMS Co., Ltd.,* 471 F.3d 1293, 1305-06 (Fed. Cir. 2006) (*en banc*).

34. Defendant’s proposed prescribing information contains a series of instructions by Defendant to doctors and patients regarding how Defendant’s ANDA Products are to be used, when and how they should be taken, and describes the associated risks and benefits. *See, e.g.*, ACC-CYC0000069-0000089 and ACC-CYC0000156-0000173.

b. <u>Contributory Infringement</u>

35. Plaintiff contends that Defendant had actual and constructive notice of the ’952 Patent prior to filing its ANDA, and were aware that the filing of Defendants’ ANDA with a request for FDA approval prior to the expiration of the ’952 Patent would constitute an act of infringement of the ’952 Patent. Plaintiffs contend that Defendant has no reasonable basis for asserting that the commercial manufacture, use, offer for sale, or sale of the Accused Products will not infringe, contribute to the infringement of, and/or induce the infringement of, the ’952 Patent. 35 U.S.C. § 271(c); *i4i Ltd. P'ship v. Microsoft Corp.*, 598 F.3d 831, 850-51 (Fed. Cir. 2010), *aff'd* 564 U.S. 91 (2011).

36. It is an act of contributory infringement to sell, offer to sell, or import a generic drug product that the seller knows will be used to perform a patented method. See 35 U.S.C. § 271(c) (“Whoever offers to sell or sells within the United States or imports into the United States . . . a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an

infringement of such patent, and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a contributory infringer.”).

37. Contributory infringement is found where: (1) there is direct infringement; (2) the accused infringer had knowledge of the patent at issue; (3) the product has no substantial noninfringing uses; and (4) the product is a material part of the invention. *Lucent Technologies, Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1320 (Fed. Cir. 2009).

38. Once a patentee has “made out a prima facie showing” that a product is not “suitable for substantial non-infringing use,” the “burden” then “shift[s]” to the accused infringer to demonstrate otherwise. *Golden Blount, Inc. v. Robert H. Peterson Co.*, 438 F.3d 1354, 1363 (Fed. Cir. 2006). An accused infringer typically must provide evidence as to how “substantial” an “alleged non-infringing would actually be.” *AstraZeneca LP v. Apotex, Inc*., 623 F. Supp. 2d 579, 605 (D.N.J. 2009), supplemented, 623 F. Supp. 2d 615 (D.N.J. 2009), and *aff’d,* 633 F.3d 1042 (Fed. Cir. 2010); *INVISTA N. Am. S.Á.R.L. v. M & G USAS C*orp., 951 F. Supp. 2d 626 (D. Del. 2013).

III. VALIDITY

39. The asserted claims of the ‘952 Patent are presumed valid. 35 U.S.C. § 282(a); *Microsoft Corp. v. i4i Ltd. P’ship*, 564 U.S. 91, 110-14 (2011).

40. To overcome this presumption, Accord must prove invalidity “by clear and convincing evidence.” *Id*.

41. The Federal Circuit has explained that “it may be harder to meet the clear and convincing burden when the invalidity contention is based upon the same argument on the same reference that the PTO already considered.” *Sciele Pharma Inc. v. Lupin Ltd*., 684 F.3d 1253, 1260–61 (Fed. Cir. 2012). “[W]hether a reference was before the PTO goes to the weight of the

evidence, and the parties are of course free to, and generally do, make these arguments to the fact finder." *Id.; see also Endo Pharm. Inc. v. Mylan Pharm. Inc*., No. 11-CV-00717 (RMB/KW), 2014 WL 334178, at *6 (D. Del. Jan. 28, 2014), motion for relief from judgment granted, No. 11-CV-717 (RMB/KW), 2014 WL 2532179 (D. Del. June 2, 2014) ("Although a defendant's burden does not change, evidence considered by the PTO may not be given the same weight as new evidence.") (citing Sciele, 684 F.3d at 1260); *Cubist Pharm., Inc. v. Hospira, Inc*., 75 F. Supp. 3d 641, 659 (D. Del. 2014), *aff'd,* 805 F.3d 1112 (Fed. Cir. 2015) ("Practically speaking, however, 'it may be harder to meet the clear and convincing burden when the invalidity contention is based upon the same argument on the same reference that the PTO already considered.'") (*citing Sciele*, 684 F.3d at 1260–61); *Tokai Corp. v. Easton Enterprises, Inc*., 632 F.3d 1358, 1367 (Fed. Cir. 2011) ("[A]lthough the standard of proof does not depart from that of clear and convincing evidence, a party challenging validity shoulders an enhanced burden if the invalidity argument relies on the same prior art considered during examination by the U.S. Patent and Trademark Office.).

A. ACCORD HAS NOT SHOWN BY CLEAR AND CONVINCING EVIDENCE THAT THE CLAIMS OF THE '952 PATENT ARE OBVIOUS

42. 35 U.S.C. § 103 specifies that "[a] patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made."

43. "Obviousness is a question of law based on underlying factual inquiries." *See, e.g., Crocs, Inc. v. Int'l Trade Comm'n*, 598 F.3d 1294, 1308 (Fed. Cir. 2010). "Whether a claim is invalid for obviousness is determined from the perspective of one of ordinary skill in the art." *See,*

e.g., Cheese Sys., Inc. v. Tetra Pak Cheese & Powder Sys., Inc., 725 F.3d 1341, 1352 (Fed. Cir. 2013); *Unigene Labs., Inc. v. Apotex, Inc*., 655 F.3d 1352, 1361 (Fed. Cir. 2011) ("A person of ordinary skill at the time of the invention interprets the prior art using common sense and appropriate perspective.").

44. Accord has the burden to "demonstrate by clear and convincing evidence that a skilled artisan would have had reason to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success from doing so." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig*., 676 F.3d 1063, 1068-69 (Fed. Cir. 2012) (internal quotation marks omitted); accord *Endo Pharm. Sols., Inc. v. Custopharm Inc*., 894 F.3d 1374, 1380-81 (Fed. Cir. 2018).

45. Obviousness "cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." *Cheese Sys., Inc. v. Tetra Pak Cheese & Powder Sys., Inc.*, 725 F.3d 1341, 1352 (Fed. Cir. 2013) (quoting ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546 (Fed. Cir. 1998)). *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd*., 719 F.3d 1346, 1361 (Fed. Cir. 2013) (internal quotations omitted). "The inventor's own path itself never leads to a conclusion of obviousness; that is hindsight. What matters is the path that the person of ordinary skill in the art would have followed." *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012); *see also Life Techs., Inc. v. Clontech Labs., Inc.*, 224 F.3d 1320, 1326 (Fed. Cir. 2000) ("That the inventors were ultimately successful is irrelevant to whether one of ordinary skill in the art, at the time the invention was made, would have reasonably expected success."); *In re Gluag*, 283 F.3d 1335, 1341 (Fed. Cir. 2002) (a factfinder may not use an inventor's "own explanation of his invention against him."); *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1073 (Fed. Cir. 2012)

("obviousness must be assessed at the time the invention was made"); Neptune Generics, LLC v. Eli Lilly & Co., 921 F.3d 1372, 1377 (Fed. Cir. 2019) ("[A] fact finder must not allow its analysis to be distorted by hindsight bias.") (*citing KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007))).

46. Obviousness is a legal question based on underlying factual determinations. *Eisai Co. Ltd. v. Dr. Reddy's Lab'ys, Ltd.*, 533 F.3d 1353, 1356 (Fed. Cir. 2008). The factual determinations include: (1) the scope and content of the prior art are to be determined, (2) differences between the prior art and the claims at issue are to be ascertained, (3) the level of ordinary skill in the pertinent art, and (4) secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc. *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966).

47. "To ascertain the scope of the prior art, a court examines 'the field of the inventor's endeavor,' . . . and 'the particular problem with which the inventor was involved,' at the 'time the invention was made. . . .' Defining the problem in terms of its solution reveals "To ascertain the scope of the prior art, a court examines 'the field of the inventor's endeavor,' . . . and 'the particular problem with which the inventor was involved,' at the 'time the invention was made. . . .' Defining the problem in terms of its solution reveals improper hindsight in the selection of the prior art relevant to obviousness." *Monarch Knitting Machinery v. Sulzer Morat GmbH*, 139 F.3d 877, 881 (Fed. Cir. 1998).

48. A party seeking to prove obviousness must specifically identify the combination(s) of prior art references upon which it is relying. See, e.g., ProBatter Sports, LLC v. Sports Tutor, Inc., 680 F. App'x 972, 975 (Fed. Cir. 2017) (affirming obviousness determination where defendant "did not identify to the district court a prior art obviousness combination on which it

relied"); *Motorola Mobility, LLC v. International Trade Commission*, 737 F.3d 1345, 1350 (Fed. Cir. 2013) (affirming obviousness determination where defendant "did not clearly identify the scope and content of the prior art that it was asserting, or provide any argument that certain prior art references render a specific claim obvious").

49. "An obviousness determination requires finding both 'that a skilled artisan would have been motivated to combine the teachings of the prior art . . . and that the skilled artisan would have had a reasonable expectation of success in doing so.'" *In re Stepan Company*, 868 F.3d 1342, 1345–46 (Fed. Cir. 2017) (citation omitted); *see also Pfizer, Inc. v. Apotex, Inc*., 480 F.3d 1348, 1361 (Fed. Cir. 2007) (a party seeking to invalidate a patent based on obviousness must demonstrate "by clear and convincing evidence that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so"). Courts "consider motivation to combine and reasonable expectation of success only 'if all the elements of an invention are found in a combination of prior art references[.]'" *PAR Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014) (internal quotation omitted).

50. A motivation to combine is an essential element of an obviousness challenge. *In re Stepan*, 868 F.3d at 1345–46; *see also In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1381 (Fed. Cir. 2016) (patent challenger must show that "a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention"); *Belden Inc. v. Berk–Tek LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015) ("[O]bviousness concerns whether a skilled artisan not only could have made but would have been motivated to make the combinations or modifications of prior art to arrive at the claimed invention."); *see also Avanir Pharm., Inc. v. Actavis S. Atlantic LLC*, 36 F. Supp. 3d 475, 499–501 (D. Del. 2014), *aff'd sub nom. Avanir Pharm.*

Inc. v. Par Pharm. Inc., 612 F. App'x 613 (Fed. Cir. 2015) (rejecting argument that lower dose for treatment was obvious when a person of skill would have no reason to recalculate a new dose, and data pointing to the safety and efficacy of the higher dose was reliable).

51. "The determination of obviousness is made with respect to the subject matter as a whole, not separate pieces of the claim." *Sanofi-Synthelabo v. Apotex, Inc*., 550 F.3d 1075, 1086 (Fed. Cir. 2008); accord *Gillette Co. v. S.C. Johnson & Son, Inc*., 919 F.2d 720, 724 (Fed. Cir. 1990); see also *Hybritech, Inc. v. Monoclonal Antibodies, Inc*., 802 F.2d 1367, 1383 (Fed. Cir. 1986) ("Focusing on the obviousness of substitutions and differences instead of the invention as a whole . . . [is] a legally improper way to simplify the difficult determination of obviousness."

52. Section "103 does not permit a court to stitch together an obviousness finding from discrete portions of prior art references without considering the references as a whole." *In re Enhanced Sec. Research, LLC*, 739 F.3d 1347, 1355 (Fed. Cir. 2014). The prior art "must be considered in its entirety, *i.e*., as a whole, including portions that would lead away from the invention." *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568 (Fed. Cir. 1987) (emphasis in original).

53. Obviousness cannot be shown if "researchers can only 'vary all parameters or try each of numerous possible choices until one possibly arrive[s] at a successful result, where the prior art [gives] either no indication of which parameters [are] critical or no direction as to which of many possible choices is likely to be successful.'" *P&G*, 566 F.3d at 996-97 (quoting *In re O'Farrell,* 853 F.2d 894, 903 (Fed. Cir. 1988) (finding that structural modifications of the lead compound were not routine and hence, not obvious because the properties of isphosphonates (a class of drugs) could not be anticipated based on their structure)); see also *Sanofi-Synthelabo v. Apotex, Inc*., 550 F.3d 1075, 1088-89 (Fed. Cir. 2008) (noting that the steps to formulate the

claimed compound were not "simple or routine" and that the unpredictability of the allocation of favorable properties rendered the claimed compound nonobvious over the prior art racemate); *Takeda*, 492 F.3d at 1360-63 (holding that there was no reasonable expectation to one of ordinary skill in the art to make specific molecular modifications); *Daiichi*, 619 F.3d at 1354-57 (holding that it was not obvious to modify a substituent on the prior art compounds since the prior art taught away from using that substituent).

54. "Obviousness may be defeated if the prior art indicates that the invention would not have worked for its intended purpose or otherwise teaches away from the invention." *Meiresonne v. Google, Inc.*, 849 F.3d 1379, 1382 (Fed. Cir. 2017) (citing *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1326 (Fed. Cir. 2009)); *In re Mouttet,* 686 F.3d 1322, 1333 (Fed. Cir. 2012) ("A reference that properly teaches away can preclude a determination that the reference renders a claim obvious."). "'A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant.'" *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1305 (Fed. Cir. 2015) (quoting *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994)) (affirming nonobviousness conclusion where patentee "produced ample evidence of teaching away and unexpected results, and that . . . evidence fully supports a conclusion of nonobviousness").

55. The fact-finder must avoid the "distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007); *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1320 (Fed. Cir. 2004) ("We note in this respect that the district court's use of an 'overall picture' and 'common sense' test of obviousness falls squarely into the hindsight trap."). "[T]he very ease with which the invention

can be understood may prompt one to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher." *In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000) (internal quotations omitted).

56. A showing that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected supports a finding of non-obviousness. *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995); *see also WBIP, LLC v. Kohler Co*., 829 F.3d 1317, 1335 (Fed. Cir. 2016) ("Doubt or disbelief by skilled artisans regarding the likely success of a combination or solution weighs against the notion that one would combine elements in references to achieve the claimed invention."); *Avanir Pharm., Inc. v. Actavis S. Atl. LLC*, 36 F. Supp. 3d 475 (D. Del. 2014), *aff'd sub nom. Avanir Pharm. Inc. v. Par Pharm. Inc*., 612 F. App'x 613 (Fed. Cir. 2015) (unexpected results support patentability).

57. The "basic principle behind this rule is straightforward—that which would have been surprising to a person of ordinary skill in a particular art would not have been obvious. The principle applies most often to the less predictable fields, such as chemistry, where minor changes in a product or process may yield substantially different results." *Soni*, 54 F.3d at 750.

58. Although unexpected results must be reasonably commensurate in scope with the claims, there is no requirement of absolute identity of scope; rather, evidence of unexpected results has been rejected only "where the evidence was plainly disproportionate to the scope of the claim." *Genetics Inst., LLC v. Novartis Vaccines & Diagnostics, Inc.*, 655 F.3d 1291, 1308 (Fed. Cir. 2011).

59. When as here invalidity is based on references that were applied by the examiner during prosecution of the patent and distinguished, it is "especially difficult" to overcome the

presumption of validity. *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1375 (Fed. Cir. 2006); *Glaxo Grp. Ltd. v. Apotex, Inc.*, 376 F.3d 1339, 1348 (Fed. Cir. 2004).

60. No presumption of obviousness applies where, as here, the "invention is contended to be obvious based upon a combination of elements across different references," the Defendant must prove that there was a motivation "for such a combination." *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1320 (Fed. Cir. 2004).

61. Plaintiffs contend that the invention of Claims 1-4 of the '952 Patent would not have been obvious-to-try. "Evidence of obviousness, especially when that evidence is proffered in support of an 'obvious-to-try' theory, is insufficient unless it indicates that the possible options skilled artisans would have encountered were 'finite,' 'small,' or 'easily traversed,' and that skilled artisans would have had a reason to select the route that produced the claimed invention." *In re Cyclobenzaprine*, 676 F.3d 1063, 1072 (Fed. Cir. 2012).

62. In *In re O'Farrell*, the Federal Circuit Court discussed two classes of situations where "obvious to try" is erroneously equated with obviousness under 35 U.S.C. § 103: 1) where a skilled artisan must "explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." and 2) where "what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful." 853 F.2d 894, 903 (Fed. Cir. 1988). In *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007), the Supreme Court held that "the fact that a combination was obvious to try might show that it was obvious" only if "there are a finite number of identified, predictable solutions"

that lead to anticipation of success. In *In re Kubin*, the Federal Circuit reaffirmed the above holdings from *In re O'Farrell* in view of *KSR*, cautioning against "erroneously equat[ing]" "obvious to try" with obviousness in the "two classes of situations" discussed above. 561 F.3d 1351, 1359 (Fed. Cir 2009) (*quoting In re O'Farrell*, 853 F.2d at 903).

63. The Federal Circuit and courts in the Third Circuit have continued to hold that obvious to try does not yield obviousness in the situations discussed in *In re O'Farrell* and when there are not a finite number of identified, predictable solutions. *See, e.g., In re Brimonidine Patent Litig*., 643 F.3d 1366, 1376 (Fed. Cir. 2011) (rejecting "obvious to try" argument because the claimed invention would not have been an expected result), *cert. denied*, 566 U.S. 905 (2012); *Sanofi-Synthelabo v. Apotex, Inc*., 550 F.3d 1075, 1089 (Fed. Cir. 2008) (rejecting "obvious to try" argument where the district court made findings "on the unexpected and unpredictable properties" of the claimed compound*); Merck & Co. v. Sandoz Inc*., 2012 WL 266412, *3–4 (D.N.J. Jan. 30, 2012) (rejecting obvious to try argument that the "claimed formulation is a result of routine pharmaceutical development, not invention," where person of ordinary skill would not have "viewed the final outcome of the process as one of a finite number of identified, predictable solutions"); *Cephalon, Inc. v. Watson Labs*., Inc. (*In re Armodafinil Patent Litig. Inc*.), 939 F. Supp. 2d 456, 501–502 (D. Del. 2013) ("'Obvious to try' is not equivalent to obviousness in every case, particularly where, as here, the prior art provided at most general motivation to conduct trial and error experimentation in a decidedly unpredictable field.") (*citing In re Kubin*, 561 F.3d at 1359–60, *In re Brimonidine Patent Litig*., 643 F.3d at 1376).

64. "Use of inherency in an obviousness context must . . . be 'carefully circumscribed' because 'that which may be inherent is not necessarily known and that which is unknown cannot be obvious.'" *Vivint, Inc. v. Alarm.com Inc*., 741 F. App'x 786, 792 (Fed. Cir. 2018) (*quoting*

Honeywell Int'l Inc. v. Mexichem Amanco Holding S.A., 865 F.3d 1348, 1354–55 (Fed. Cir. 2017)); *PAR Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1195 (Fed. Cir. 2014) ("We have, however, also explained that the use of inherency, a doctrine originally rooted in anticipation, must be carefully circumscribed in the context of obviousness."); *id*. at 1195 ("A party must, therefore, meet a high standard in order to rely on inherency."). "Thus, while [the Federal Circuit] ha[s] recognized that 'inherency may supply a missing claim limitation in an obviousness analysis,' we have emphasized that 'the limitation at issue necessarily must be present, or the natural result of the combination of elements explicitly disclosed by the prior art.'" *Id*. (*quoting Par*, 773 F.3d at 1194–96 (emphasis in original)).

1. Objective Indicia of Nonobviousness

65. Objective indicia of nonobviousness constitute independent evidence of nonobviousness and enable courts to avoid hindsight. *Millennium Pharm., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1367-1368 (Fed. Cir. 2017). Often, these objective factors are the "most probative and cogent evidence in the record," and must always be considered as part of the original determination of obviousness. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538–39 (Fed. Cir. 1983) (citations omitted).

66. "The objective considerations, when considered with the balance of the obviousness evidence in the record, guard as a check against hindsight bias." *Cyclobenzaprine*, 676 F.3d at 1079 (citing *Graham*, 383 U.S. at 36); *see also, Graham*, 383 U.S. at 36 ("These legal inferences or subtests do focus attention on economic and motivational rather than technical issues and are, therefore, more susceptible of judicial treatment than are the highly technical facts often present in patent litigation.") (citing Note, Subtests of 'Nonobviousness': A Nontechnical Approach to Patent Validity, 112 U. Pa. L. Rev. 1169 (1964)).

67. Objective evidence of nonobviousness is to be considered as part of all the evidence, "not just when the decisionmaker remains in doubt after reviewing the art." *Stratoflex*, 713 F.2d at 1538–39; *see also Cyclobenzaprine*, 676 F.3d at 1077. Thus, when the patentee comes forward with evidence of objective indicia, the defendant must demonstrate that the claims were obvious in light of all the evidence by clear and convincing evidence. *See Stratoflex*, 713 F.2d at 1538–39; *see also Cyclobenzaprine*, 676 F.3d at 1079–80 ("[O]pinions of this court should not be read to require a burden-shifting framework in derogation of Stratoflex's directive that objective evidence be considered before making an obviousness determination and in disregard of where the burdens of proof and persuasion are properly placed in district court litigation."). The "burden of persuasion" remains with the patent challenger. *Id*. at 1078.

68. "Evidence of secondary considerations must be reasonably commensurate with the scope of the claims." *In re Huai-Hung Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011) (citations omitted). "This does not mean that an applicant is required to test every embodiment within the scope of his or her claims. If an applicant demonstrates that an embodiment has an unexpected result and provides an adequate basis to support the conclusion that other embodiments falling within the claim will behave in the same manner, this will generally establish that the evidence is commensurate with the scope of the claims." *Id.* (citations omitted).

69. Even where the claim is much broader than the embodiment to which the evidence of secondary considerations pertains, that evidence must be afforded "some weight, taking into account the degree of the connection between the features presented in the evidence and the elements recited in the claims*." ClassCo, Inc. v. Apple, Inc.*, 838 F.3d 1214, 1221 (Fed. Cir. 2016) (emphasis in original); *see also Cadence Pharm., Inc. v. Exela Pharma Scis., LLC*, 2013 WL 11083853, at *29 (D. Del. Nov. 14, 2013) (holding that there was a nexus between the commercial

products and the patent where the patent claims required a "stable formulation," a novel feature of the patent, and the commercial products were "stable formulations" within the meaning of the patent).

70. In order to accord substantial weight to secondary considerations in an obviousness analysis, "the evidence of secondary considerations must have a 'nexus' to the claims, i.e., there must be 'a legally and factually sufficient connection' between the evidence and the patented invention." *Fox Factory, Inc. v. SRAM, LLC*, 944 F.3d 1366, 1373 (Fed. Cir. 2019). A nexus exists where there is a link between the objective indicia and the claimed invention. *See, e.g., Vicor Corp. v. SynQor, Inc.*, 869 F.3d 1309, 1315 (Fed. Cir. 2017); *SynQor, Inc. v. Artesyn Techs., Inc.*, 709 F.3d 1365, 1372, 1374 (Fed. Cir. 2013) (*SynQor I*).

71. As the Federal Circuit first recognized in *Demaco Corp. v. F. Von Langsdorff Licensing Ltd*., a patentee is entitled to a rebuttable presumption of nexus between the asserted evidence of secondary considerations and a patent claim if the patentee shows that the asserted evidence is tied to a specific product and that the product "is the invention disclosed and claimed." 851 F.2d 1387, 1392 (Fed. Cir. 1988). That is, presuming nexus is appropriate "when the patentee shows that the asserted objective evidence is tied to a specific product and that product 'embodies the claimed features, and is coextensive with them.'" *Polaris Indus., Inc. v. Arctic Cat, Inc.*, 882 F.3d 1056, 1072 (Fed. Cir. 2018) (quoting *Brown & Williamson Tobacco Corp. v. Philip Morris Inc*., 229 F.3d 1120, 1130 (Fed. Cir. 2000)).

72. Because the Ingenus NDA Products embody the '952 Patent claims, nexus is presumed and the burden shifts to Defendant to rebut the presumed nexus. *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc*., 364 F. Supp. 2d 820, 907 (S.D.In. 2005)("If the marketed product embodies the claimed features, and is coextensive with them, then a nexus is presumed and the

burden shifts to the party asserting obviousness to present evidence to rebut the presumed nexus." *Id.*, citing *Brown & Williamson*, 229 F.3d at 1130.

73. With respect to unexpected results, “[a] nexus does not require that a claim expressly recite the advantages of the patented invention; it is enough that they flow directly from the invention.” *Valeant Int'l (Barbados) SRL v. Watson Pharm., Inc.*, No. 10-20526-CIV, 2011 WL 6792653, at *11 (S.D. Fla. Nov. 8, 2011), *aff’d sub nom. Valeant Int’l Bermuda v. Actavis, Inc*., 534 F. App’x 999 (Fed. Cir. 2013) (citing *Preemption Devices, Inc. v. Minnesota Mining & Mfg. Co*., 732 F.2d 903, 907 (Fed. Cir. 1984)).

74. The existence of a long-felt but unsolved need that is met by a claimed invention is objective evidence of non-obviousness. *Millennium*, 862 F.3d at 1369. This is because it is reasonable to infer that the need would have not persisted had the solution been obvious. *WBIP, LLC v. Kohler Co*., 829 F.3d 1317, 1332 (Fed. Cir. 2016).

75. A long-felt, but unsolved need provides evidence of non-obviousness. *Ecolochem, Inc. v. S. Cal. Edison Co*., 227 F.3d 1361, 1376-77 (Fed. Cir. 2000); see also *In re Dow Chem. Co*., 837 F.2d 469, 472 (Fed. Cir. 1988) (“Recognition of need, and difficulties encountered by those skilled in the field, are classical indicia of unobviousness.”) (citing *Graham*, 383 U.S. at 17; *Custom Accessories v. Jeffrey-Allan Indus*., 807 F.2d 955, 960 (Fed. Cir. 1986)); *Monarch Knitting*, 139 F.3d at 884.

76. An alleged prior art solution to a long felt need must be an available product. *Janssen Pharms., Inc. v. Teva Pharms. USA, Inc.*, No. 2:18-00734, 2024 U.S. Dist. LEXIS 227696 (D.N.J. December 17, 2024)(“Teva also argues that the '548 Protocol had already solved this long-felt need. [ ] But the '548 Protocol "is not an available product," and thus could not have been the solution, [citing] *Millennium Pharms., Inc. v. Sandoz Inc*., 862 F.3d 1356, 1369 (Fed. Cir. 2017)

(holding it was clear error to find that long-felt need was solved by a prior art compound that was not commercially available)").

77. "Courts look to the ***availability*** and sufficiency of the prior art methods to meet the need of the claimed invention—not merely whether there was a motivation to improve upon an existing method." *Pacira Pharms., Inc. v. eVenus Pharms. Labs., Inc*., No. 21-19829, 2024 U.S. Dist. LEXIS 144544 at *36 (D.N.J. August 9, 2024) (emphasis added).

78. Unexpected results are objective evidence of nonobviousness because "that which would have been surprising to a person of ordinary skill in a particular art would not have been obvious." *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995).

79. Accord copied the formulations of Plaintiffs' NDA Products in Accord's ANDA Products (ACC-CYC0000305-307), which is probative of nonobviousness. *Forest Labs., Inc. v. Ivax Pharms., Inc*., 438 F. Supp. 2d 479 (D. Del. 2006); *Bayer Pharma AG v. Watson Labs., Inc.*, 183 F. Supp. 3d 538, 550 (D. Del. 2016).

80. Accord did not seek to copy other formulations of cyclophosphamide, *e.g.* powdered or lyophilized formulations, in its ANDA. *Forest Labs., Inc. v. Ivax Pharms., Inc*., 438 F. Supp. 2d 479 (D. Del. 2006)("In the Court's view, the copying of others is particularly telling in this case, because citalopram is currently available as a generic drug. Indeed, citalopram is sold generically by Defendants, yet Defendants seek to copy and sell Lexapro(R). Further, five generic drug manufacturers have sought approval to market generic escitalopram products despite the fact that they are already making or can make generic citalopram.").

81. Accord's ANDA included same the active ingredient (cyclophosphamide) and the same inactive ingredients (ethanol, polyethylene glycol, propylene glycol, and monothioglycerol) in the same amounts and mass ratios as Plaintiffs' NDA Products. *Merck Sharp & Dohme Corp.*

v. Hospira Inc., 221 F. Supp. 3d 497 (D. Del. 2016) ("Defendant is correct that 21 U.S.C. § 355(j)(2)(A) requires a generic to copy the active pharmaceutical ingredient of the reference drug, and to establish bioequivalency. The generic is not, however, required to copy inactive ingredients or the methods used in a manufacturing process. . . . Defendant's decision to copy Plaintiff's formulation and process "is an indicium of nonobviousness.").

82. Accord could have developed a lyophilized formulation of cyclophosphamide, but one of the factors it considered in copying Plaintiffs formulations was whether U.S. sales met a $10 million threshold. *Merck Sharp & Dohme Corp. v. Sandoz Inc.*, No. 3:12-cv-032892015 U.S. Dist. LEXIS 113710 (D.N.J. Aug. 27, 2015)((the evidence of copying to be compelling where the generic company had the option to market one version of the active ingredient in the same market, but continued to pursue a separately patented, prodrug version because it could "make a profit at selling" it.).

83. Accord considered, but rejected, several noninfringing alternatives to Plaintiffs' NDA product before deciding to copy it. *Bayer Pharma AG v. Watson Labs., Inc.*, 183 F. Supp. 3d 538, 550 (D. Del. 2016)(copying of an ANDA product held to be probative of non-obviousness when it showed that the defendant considered but rejected design-around alternatives of the claimed formulations), *rev'd on other grounds, Bayer Pharma AG v. Watson Labs., Inc.*, 874 F.3d 1316 (Fed. Cir. 2017).

84. Copying of claim elements that the Hatch-Waxman Act does not require the generic manufacturer to copy is probative of nonobviousness. *Dey, L.P. v. Teva Parenteral Medicines, Inc.*, 6 F. Supp. 3d 651, 681 (N.D.W. Va. 2014), aff'd, 600 F. App'x 773 (Fed. Cir. 2015) (copying by a generic, where there is no regulatory requirement to do so, "provides a strong indication that the prior art provided Teva with no obvious alternative to [the] invention"); *Sanofi-Aventis*

Deutschland GmbH v. Glenmark Pharm., Inc., USA, No. 07-CV-5855 DMCJAD, 2011 WL 383861, at *9 (D.N.J. Feb. 3, 2011) (same).

85. Plaintiffs contend that a person having ordinary skill in the art at the time of the invention of Claims 1-4 of the '952 Patent would not have concluded that the invention would have been obvious from the prior art cited by Defendant.

2. <u>Issues of Law Relating to Obviousness</u>

86. Plaintiffs contend that the following issues of law relating to obviousness remain to be litigated:

i. Whether a person having ordinary skill in the art at the time of the invention would conclude that there is motivation to combine the prior art formulations of Alam, Palepu, Shaik, Sauerbier and Tait to arrive at the invention of the stable liquid parenteral formulation of cyclophosphamide as recited in Claims 1-4 of the '952 Patent.

ii. Whether the conclusion that Claims 1-4 of the '952 Patent would have been obvious to a person having ordinary skill in the art at the time of the invention is based upon an impermissible hindsight reconstruction of the claimed invention.

iii. Whether a person of ordinary skill in the art at the time of the invention of the '952 Patent would have concluded that the concentration of cyclophosphamide recited in Claim 1 ("about 12% to about 23%") could be obtained by optimizing the disclosures of the prior art references (Alam, Palepu, Shaik, Sauerbier and Tait).

iv. Whether it would have been obvious for a person of ordinary skill in the art at the time of the invention of the '952 Patent to select a concentration of ethanol content of "about 70% to about 75%" based upon Palepu, Shaik, Saubier and Tait, through routine experimentation.

v. Whether it would have been obvious from Alam, Palepu, Shaik and Tait and through experimentation with relative amounts of polyethylene glycol and propylene glycol for a person of ordinary skill in the art at the time of the invention of the '952 Patent to arrive at a stable liquid parenteral formulation of cyclophosphamide as recited in Claim 1 of the '952 Patent requiring "iii) both polyethylene glycol and propylene glycol, wherein a polyethylene glycol to propylene glycol mass ratio is between approximately 1.0:1.0 to approximately 2.0:1.0; and iv) about 3.4% to about 8.8% based on total formulation weight of polyethylene glycol [and] v) about 3.4% to about 4.4% based on total formulation weight of propylene glycol."

vi. Whether it would have been obvious for a person of ordinary skill in the art at the time of the invention of the '952 Patent to modify the formulations of cyclophosphamide described in Alam, Palepu, Shaik and Tait so that "after storage for 7 days at 40° C./75% RH, decomposition to form any of the following impurities is less than 0.5%: a) bis(2-chloroethyl)amine hydrochloride; b) 3-(2-chloroethyl)-2-oxo-2-hydroxy-l ,3,6,2-oxadiazaphosphonane; and c) 3-[2-(2-chloroethylamino)ethyl amino] propyl dihydrogen phosphate dihydrochloride" and thereby arrive at a

stable liquid parenteral formulation of cyclophosphamide as recited in Claim 1 of the ‘952 Patent.

vii. Whether the experimental data relied upon by the applicant during the prosecution of the ‘952 Patent in which the claimed formulations where compared to the closest prior art demonstrate an unexpected improvement in stability of the liquid parenteral formulation of cyclophosphamide recited in Claims 1-4 as confirmed by the examiner in her Statement of Reasons for Allowance. (“Applicant has shown (Tables, pages 4-5, Declaration of 15 January 2021), in a side-by-side comparison, that *better stability* (less impurities formed and smaller % assay drop after 1 week at 40˚C) is achieved . . .” with the claimed formulations.) Dkt. 34-1 at 563 (J.A._561).

viii. Whether there are indicia of nonobviousness of the stable liquid parenteral formulation of cyclophosphamide of Claims 1-4 of the ‘952 Patent which overcomes any possible *prima facie* case of obviousness based upon Alam, Palepu, Shaik, Sauerbier and/or Tait including: the existence of a long-felt but unsolved need of known cyclophosphamide formulations that is met by the claimed invention; failure of others to provide a feasible solution to longstanding problems with known cyclophosphamide formulations; unexpected results relating to stability of the liquid parenteral formulation of cyclophosphamide of the claimed invention; and copying of the claimed invention by others when alternatives were available.

B. ACCORD CANNOT ESTABLISH BY CLEAR AND CONVINCING EVIDENCE THAT THE '952 PATENT SPECIFICATION FAILS TO DEMONSTRATE THAT THE INVENTOR POSSESSED THE INVENTION

87. Accord cannot establish that Claims 1-4 of the '952 Patent are invalid under 35 U.S.C. § 112(a) for lack of written description.

88. 35 U.S.C. § 112(a) requires that the specification contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention. 35 U.S.C. § 112(a).

89. Whether a claim satisfies the written description requirement is a question of fact. *Alcon Research Ltd. v. Barr Labs., Inc*., 745 F.3d 1180, 1190 (Fed. Cir. 2014).

90. The test for written description is "whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art. Based on that inquiry, the specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed." *Id.* Whether the written description requirement is met for a particular claim or claims is a question of fact. *Glaxo Smith Kline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725, 729 (Fed. Cir. 2014).

91. "There is no rigid requirement that the disclosure contain 'either examples or an actual reduction to practice'; the proper inquiry is whether the patentee has provided an adequate description that 'in a definite way identifies the claimed invention' in sufficient detail such that a person of ordinary skill would understand that the inventor had made the invention at the time of

filing." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1344 (Fed. Cir. 2010) (en banc). "That assessment 'requires an objective inquiry into the four corners of the specification,' as 'the hallmark of written description is disclosure.'" *Id*. at 1351.

92. "The [written description] requirement is applied in the context of the state of knowledge at the time of the invention." *Capon v. Eshhar*, 418 F.3d 1349, 358 (Fed. Cir. 2005); *see also MorphoSys AG v. Janssen Biotech, Inc*., 358 F. Supp. 3d 354, 364 (D. Del. 2019) (quoting Ariad, 598 F.3d at 1351) ("The adequacy of [a patent's written description] disclosure is evaluated in view of 'the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.'").

93. As such, "[t]he written description 'need not include information that is already known and available to the experienced public.'" *Zoltek Corp. v. United States*, 815 F.3d 1302, 1308 (Fed. Cir. 2016) (quoting *Space Sys./Loral, Inc. v. Lockheed Martin Corp*., 405 F.3d 985, 987 (Fed. Cir. 2005)); see also *Streck, Inc. v. Research & Diagnostic Sys., Inc*., 665 F.3d 1269, 1285 ("Given this perspective [of a POSA], in some instances, a patentee can rely on information that is 'well-known in the art' to satisfy written description.") (citing *Boston Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1366 (Fed. Cir. 2011)); *In re Eltgroth*, 57 C.C.P.A. 833, 419 F.2d 918, 921 (C.C.P.A. 1970) ("This court has often observed that minutiae of descriptions or procedures perfectly obvious to one of ordinary skill in the art yet unfamiliar to laymen need not be set forth.").

94. The Federal Circuit has long held that "to satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue." *Crown Operations Intern., Ltd. v. Solutia Inc*., 289 F.3d 1367, 1376 (Fed. Cir. 2002); *see also Application of Smith*, 481 F.2d 910, 914 (C.C.P.A. 1973) ("[C]laimed subject matter need not be described in haec verba in the specification in order for

that specification to satisfy the description requirement . . . ."). Instead, "one skilled in the art, reading the original disclosure, must reasonably discern the limitation at issue in the claims." *Id.*

95. The written description requirement does not demand "either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement." *Streck*, 665 F.3d at 1285 (quoting *Ariad*, 598 F.3d at 1352); *Avanir Pharm., Inc. v. Actavis S. Atl. LLC*, 36 F. Supp. 3d 475, 509 (D. Del. 2014), *aff'd sub nom. Avanir Pharm. Inc. v. Par Pharm. Inc*., 612 F. App'x 613 (Fed. Cir. 2015) (rejecting defendants' written description argument because "it improperly require[d] working examples to satisfy written description"). The patent needs to contain only a sufficient description of the invention to convey to a person of ordinary skill in the art that the inventor was in possession of the invention. *Ariad*, 598 F.3d at 1.

96. Plaintiffs contend that a person having ordinary skill in the art would conclude that the inventors of the '952 Patent had possession of the subject matter of Claims 1-4 of the '952 Patent at the time of the invention.

1. Issues of Law Relating to Written Description

97. Plaintiffs contend that the following issue of law relating to written description remains to be litigated:

i. Whether the specification of the '952 Patent, the "four corners" of which provide *inter alia* several examples of the claimed stable liquid parenteral formulations of cyclophosphamide and stability testing of certain of those formulations under accelerated conditions for a period of 1 week at 40° C. and 75% RH, provides sufficient detail such that a person of ordinary skill

would understand that the inventors had made the claimed invention at the time of filing.

C. ACCORD CANNOT ESTABLISH BY CLEAR AND CONVINCING EVIDENCE THAT THE '952 PATENT FAILS TO TEACH A PERSON OF ORDINARY SKILL HOW TO MAKE AND USE THE INVENTION

98. Accord cannot establish that Claims 1-4 of the '952 Patent are invalid under 35 U.S.C. § 112(a) for lack of enablement.

99. Enablement is a question of law that is based on underlying factual inquiries. *Cephalon, Inc. v. Watson Pharms., Inc*., 707 F.3d 1330, 1336 (Fed. Cir. 2013).

100. The claims of a patent are presumed to be enabled. *Cephalon, Inc. v. Watson Pharm., Inc*., 707 F.3d 1330, 1337 (Fed. Cir. 2013). Those alleging invalidity based on lack of enablement have the burden to overcome this presumption by showing clear and convincing evidence of nonenablement. *Id.* ("Because we must presume a patent enabled, the challenger bears the burden, throughout the litigation, of proving lack of enablement by clear and convincing evidence.") (citing *Morton Int'l, Inc. v. Cardinal Chem. Co*., 5 F.3d 1464, 1469–70 (Fed. Cir. 1993)). The evidence of non-enablement must be more than *ipse dixit* from an expert. *Cephalon*, 707 F.3d at 1338.

101. The enablement requirement "is met when at the time of filing the application one skilled in the art, having read the specification, could practice the invention without 'undue experimentation.'" *Id*. at 1336 (quoting *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988)). "Whether undue experimentation is required 'is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations.'" *Id*. at 1336 (quoting *ALZA Corp. v. Andrx Pharms*., LLC, 603 F.3d 935, 940 (Fed. Cir. 2010).

102. "The following factors may be considered in determining whether a disclosure would require undue experimentation: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance needed; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. *Id*. at 1336 (citing *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988)).

103. "[T]he specification need not include a working example of every possible embodiment to enable the full scope of the claims." *Bayer Healthcare LLC v. Baxalta, Inc*., 989 F.3d 964, 982 (Fed. Cir. 2021) (citation omitted). On the contrary "whether a patent is enabled—or requires undue experimentation—are questions that must be viewed "from the perspective of one of ordinary skill in the art." *Id*. (citing *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1365 (Fed. Cir. 2006)).

104. "[A] considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance." *Cephalon*, 707 F.3d at 1339; *Eli Lilly & Co. v. Actavis Elizabeth LLC*, 435 F. App'x 917, 923 (Fed. Cir. 2011); *Enzo Biochem, Inc. v. Calgene Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999)).

105. As a threshold matter, the patent challenger must first make a "threshold showing that any experimentation is necessary" before the Court determines "whether the amount of that experimentation is either 'undue' or sufficiently routine." *Alcon*, 745 F.3d at 1188–89 (holding that the district court mistakenly "appl[ied] the *Wands* factors as if they were a generalized test for deciding whether a patent disclosure is sufficiently detailed to support a broad claim").

106. "[A] patent need not teach, and preferably omits, what is well known in the art." *Hybritech*, 802 F.2d at 1384 (citing *Lindemann Maschinenfabrik v. American Hoist and Derrick*,

730 F.2d 1452, 1457 (Fed. Cir. 1984)); *see also* MPEP § 2164.05(a) (citing cases); *see also, e.g., Storer v. Clark*, 860 F.3d 1340, 1350 (Fed. Cir. 2017) (in Section 112 context, "[k]nowledge of the prior art is presumed, as well as skill in the field of the invention"); *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1365 (Fed. Cir. 2006) ("The person of ordinary skill in the art would clearly have possessed such knowledge [of "application publications in professional journals" at the time the application was filed], and given the ready accessibility of the journals, the absence of incorporation by reference is not problematic. Indeed, '[a] patent need not teach, and preferably omits, what is well known in the art.'") (quoting *Spectra–Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987)). Thus, the law does not require a specification to set forth what is already in the prior art, and in fact discourages patent applicants from doing so.

107. 90. "[A] patent does not need to guarantee that the invention works for a claim to be enabled. It is well settled that an invention may be patented before it is actually reduced to practice." *Alcon*, 745 F.3d at 1189 (quoting *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 61 (1998)). In *Alcon*, the Federal Circuit explained that:

> Similarly, a patentee is not required to provide actual working examples; [the Federal Circuit has] rejected enablement challenges based on the theory that there can be no guarantee that prophetic examples actually work, as "[t]he burden is on one challenging validity to show by clear and convincing evidence that the prophetic examples together with other parts of the specification are not enabling." Nor is it "a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works." Thus, it is likewise irrelevant [], as a legal matter, whether the [] patents contain data proving that [the compounds function as claimed].

Id. at 1189–90 (citations omitted).

108. "Enablement does not require an inventor to meet lofty standards for success in the commercial marketplace. Title 35 does not require that a patent disclosure enable one of ordinary

skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect." *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338 (Fed. Cir. 2003).

109. "'A specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.'" *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995) (quoting *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 223 (C.C.P.A. 1971)) (emphases in original); *see also GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 2013 WL 4082232, at *22 (D. Del. Aug. 9, 2013), aff'd, 744 F.3d 725 (Fed. Cir. 2014).

110. Plaintiffs contend that a person having ordinary skill in the art would conclude that Claims 1-4 of the '952 Patent are enabled by the specification and would not require undue experimentation in order to practice the invention.

1. <u>Issues of Law Relating to Enablement</u>

111. Plaintiffs contend that the following issue of law relating to enablement remains to be litigated:

i. Whether the specification of the '952 Patent which *inter alia* provides several examples of the claimed stable liquid parenteral formulations of cyclophosphamide and stability testing under accelerated conditions for a period of 1 week at 40° C./75% RH provides adequate enablement for Claims 1-4 of the '952 Patent without undue experimentation.

D. ACCORD CANNOT ESTABLISH THAT CLAIMS 1-4 OF THE '952 PATENT FAIL TO INFORM A PERSON OF ORDINARY SKILL IN THE ART ABOUT THE SCOPE OF THE CLAIMS

112. Accord cannot establish by clear and convincing evidence that Claims 1-4 of the '952 Patent are invalid under 35 U.S.C. § 112(b) for indefiniteness.

113. 35 U.S.C. § 112(b), requires that the patent specification conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

114. To comply with 35 U.S.C. § 112(b), "a patent's claims, viewed in light of the specification and prosecution history, [must] inform those skilled in the art about the scope of the invention with reasonable certainty." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 910 (2014).

115. Plaintiffs contend that the terms "ethanol content of about 70% to about 75%" and "cyclophosphamide in a concentration of about 12% to about 23%" (Claim 1) and "an ethanol content of about 70% based on total formulation weight" and "about 23%" cyclophosphamide" (Claim 4) have clear, plain and ordinary meanings that inform a person of ordinary skill in the art of the scope of the asserted claims.

116. Plaintiffs further contend that a person having ordinary skill in the art would understand that "about" means exactly what it says – an ethanol content of about 70% to about 75% – and while 70% and 75% are numerical ends of the claimed range, the term "about" provides some scope of claim coverage beyond the strict numerical end points recited

1. <u>Issues of Law Relating to Indefiniteness</u>

117. Plaintiffs contend that the following issue of law relating to indefiniteness remains to be litigated:

i. Whether the following limitations of Claims 1-4 of the 952 Patent when viewed in light of the specification and prosecution history inform a person skilled in the art about the scope of the invention with reasonable certainty:

Claim 1 – "an ethanol content of about 70% to about 75% based on total formulation weight" and "cyclophosphamide in a concentration of about 12% to about 23%"; and

Claim 4 – "an ethanol content of about 70% based on total formulation weight" and "about 23%" cyclophosphamide."

E. PLAINTIFFS ARE ENTITLED TO AN INJUNCTION PRECLUDING ACCORD FROM SELLING ITS GENERIC CYCLOPHOSPHAMIDE PRODUCTS BEFORE THE '952 PATENT-IN-SUIT EXPIRES

118. "Under 35 U.S.C. § 271(e)(2), a generic manufacturer infringes a patent by filing an ANDA to obtain approval for a generic drug product claimed by a valid and unexpired patent." *Eli Lilly & Co. v. Teva Pharm. USA, Inc.*, 557 F.3d 1346, 1348 (Fed. Cir. 2009).

119. Section 271(e)(4)(A) provides that for an act of infringement under section 271(e)(2), "the court shall order the effective date of any approval of the drug . . . involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed . . ." 35 U.S.C. § 271(e)(4)(A).

120. Section 271(e)(4)(B) provides that for an act of infringement under section 271(e)(2), "injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug. . . ." 35 U.S.C. § 271(e)(4)(B).

121. Accord's proposed cyclophosphamide product infringes the asserted claims of the '952 patent. The asserted claims of the '952 patent are valid and enforceable. Accord should

therefore be enjoined from commercially manufacturing, using, offering for sale, selling, or importing its proposed cyclophosphamide for injection product prior to the expiration of the ’952 patent, including any associated extensions and exclusivities.

IV. THIS IS AN EXCEPTIONAL CASE

122. 35 U.S.C. § 285 entitles prevailing patent litigants to attorneys’ fees in “exceptional” cases. The Supreme Court relaxed the standard for what cases may be considered exceptional. *Octane Fitness, LLC v. Icon Health & Fitness, Inc*., 134 S.Ct. 1749, 1756 (2014). Under Octane, “an ‘exceptional’ case is simply one that stands out from others with respect to the substantive strength of a party’s litigation position (considering both the governing law and the facts of the case) or the unreasonable manner in which the case was litigated.” *Id.* District courts “may determine whether a case is ‘exceptional’ in the case-by-case exercise of their discretion, considering the totality of the circumstances.” *Id*. Patent litigants must establish entitlement to attorney fees under 35 U.S.C. § 285 by a preponderance of evidence. Id. at 1758.

123. In *pre-Octane* Hatch-Waxman cases, awards of attorneys’ fees under § 285 were found to be appropriate where the generic manufacturer lacked a legitimate basis for claiming a patent was invalid for obviousness or engaged in litigation misconduct. *See Takeda Chem. Indus., Ltd. v. Mylan Labs., Inc*., 549 F.3d 1381, 1388-90 (Fed. Cir. 2008); *Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1346-48 (Fed. Cir. 2000).

124. Defendant has failed to prove by clear and convincing evidence that the asserted claims of the ’952 patent would have been obvious to one of ordinary skill in the art at the time invention was made in view of the prior art.

125. Defendant has failed to prove by clear and convincing evidence that the asserted claims of the ’952 patent do not satisfy the enablement or written description requirements under 35 U.S.C. §112.

126. Defendant has failed to prove by clear and convincing evidence that the claims of the ’952 patent are invalid for indefiniteness under 35 U.S.C. § 112.

127. Defendant has maintained a meritless noninfringement position throughout this case, while representing to the FDA in its ANDA a batch formulation for its commercial products that is identical to one the patent examiner stated was specifically encompassed by the claims.

EXHIBIT 5

ACCORD'S PROPOSED CONCLUSIONS OF LAW

UNREDACTED PUBLIC VERSION

TABLE OF CONTENTS

I. LEGAL PRINCIPLES 1

A. INDEFINITENESS 1

B. NONINFRINGEMENT 2

1. Literal Infringement 4

2. Infringement under the doctrine of equivalents 4

C. OBVIOUSNESS 5

D. WRITTEN DESCRIPTION 12

E. ENABLEMENT 13

II. THE ASSERTED CLAIMS ARE NOT INFRINGED 14

III. THE ASSERTED CLAIMS ARE INVALID FOR OBVIOUSNESS 15

IV. THE ASSERTED CLAIMS ARE INVALID FOR LACK OF WRITTEN DESCRIPTION AND ENABLEMENT UNDER 35 U.S.C. §112 15

ACCORD'S PROPOSED CONCLUSIONS OF LAW

I. LEGAL PRINCIPLES

A. Indefiniteness

1. A "patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc. v. Biosig Instruments, Inc*., 572 U.S. 898, 901 (2014). "The claims, when read in light of the specification and the prosecution history, must provide objective boundaries for those of skill in the art." *Interval Licensing LLC v. AOL, Inc*., 766 F.3d 1364, 1371 (Fed. Cir. 2014).

2. While the use of "about" does not automatically render a claim indefinite, "about" terms can defeat the certainty provided by numerical limitations, especially when claims are narrowed to avoid prior art. *See Amgen, Inc. v. Chugai Pharm. Co*., 927 F.2d 1200 (Fed. Cir. 1991) (applying pre-*Nautilus* more lenient "insolubly ambiguous" standard, but still finding claims indefinite where "nothing in the specification, prosecution history, or prior art provides any indication as to what range of specific activity is covered by the term 'about,' and "no expert testified as to a definite meaning for the term in the context of the prior art"); *Synthes (USA) v. Smith & Nephew, Inc*., 547 F. Supp. 2d 436, 454 (E.D. Pa. 2008) (term "less than about 2%" indefinite under insolubly ambiguous standard because "a competitor whose plate has a bone contact area-to-lower surface area ratio of 2.5%, or even 3% or 4%, would not know if he is infringing because there is no indication how much above the 2% threshold the claims at issue actually include").

3. Nor does simply using the substitute "approximate" for "about" provide the required certainty:

> The Patent's claims are entirely unhelpful to a skilled artisan. The Court cannot simply adopt Enviro Tech's construction of "about" to mean "approximately" and call it a day. Neither "about" nor "approximately" inform competitors of the Patent's scope. There's no way to know, for example, at what point a pH level is high enough to no longer be considered "about 10." Thus, the claims themselves give no indication as to how far one may deviate from the target pH level and stay within the scope of the Patent.

Enviro Tech Chem. Servs., Inc. v. Safe Foods Corp., No. 4:21-CV-00601-LPR, 2022 WL 17721179, at *13 (E.D. Ark. Dec. 15, 2022).

4. Silence from the specification coupled with conflicting possibilities may render a claim indefinite. *See Enviro*, 2022 WL 17721179, at *14 (claims indefinite where "[a]t no point does the specification explicitly attempt to define the permissible level of deviation" and the examples "give conflicting directions.").

B. Noninfringement

5. Submission of an Abbreviated New Drug Application ("ANDA") is a technical act of infringement "if the purpose of such submission is to obtain approval . . . to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent . . . before the expiration of such patent." 35 U.S.C. § 271(e)(2).

6. A Hatch-Waxman plaintiff must show, using "traditional patent infringement analysis," that actual infringement will occur if the product proposed by the ANDA applicant is brought to market. *Warner-Lambert*, 316 F.3d 3d 1348, 1365 (Fed. Cir. 2003); *see also Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569 (Fed. Cir. 1997) ("Under § 271(e)(2)(A), a court must determine whether, if the drug were approved based upon the ANDA, the manufacture, use, or sale of that drug would infringe the patent in the conventional sense.").

7. "Because drug manufacturers are bound by strict statutory provisions to sell only those products that comport with the ANDA's description of the drug, the ANDA itself dominates

the [infringement] analysis." *Ferring B.V. v. Watson Labs., Inc.-Florida*, 764 F.3d 1401, 1408 (Fed. Cir. 2014) (internal quotations and citations omitted); see also *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1186 (Fed. Cir. 2014).

8. Further, a plaintiff "cannot meet its burden of proving infringement solely on the basis of quality control specifications contained in an ANDA." *Glaxo Inc. v. Boehringer Ingelheim Corp.*, 954 F. Supp. 469, 474 (D. Conn. 1996).

9. Plaintiff bears the burden of proving infringement by a preponderance of the evidence, and the burden of proof does not shift to the ANDA filer merely by the filing of the ANDA. *See Glaxo*, 110 F.3d. at 1568, 1570.

10. A patent infringement analysis is a two-step process. "The first step is determining the meaning and scope of the patent claims asserted to be infringed." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). In the second step, the accused device must be compared to the claims as properly construed. *See id.*; *Tanabe Seiyaku Co. v. U.S. Int'l Trade Comm'n*, 109 F.3d 726, 731 (Fed. Cir. 1997).

11. To establish infringement of a patent claim, every limitation set forth in the patent claim must be found in the accused product or process either literally or by a substantial equivalent. *See, e.g., Starhome GmbH v. AT&T Mobility LLC*, 743 F.3d 849, 858 (Fed. Cir. 2014).

12. Because a dependent claim incorporates all the limitations of the independent claim from which it depends, any dependent claim cannot be infringed unless each and every element of the independent claim is also infringed. 35 U.S.C. § 112; ¶ 4; *see Ferring*, 764 F.3d at 1411; *Jeneric/Pentron, Inc. v. Dillon Co., Inc.*, 205 F.3d 1377, 1383 (Fed. Cir. 2000); *Wahpeton Canvas Co. Inc. v. Frontier, Inc.*, 870 F.2d 1546, 1552, n. 9 (Fed. Cir. 1989).

1. Literal Infringement

13. Literal infringement requires the patentee to prove by a preponderance of the evidence that each and every limitation of the asserted claims is present in the allegedly infringing products. *Biovail Corp. Int'l v. Andrx Pharms., Inc.*, 239 F.3d 1297, 1302 (Fed. Cir. 2001); *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1247 (Fed. Cir. 2000).

2. Infringement under the doctrine of equivalents

14. A product or process that does not literally infringe a patent based on the express terms of the patent claims may nonetheless be found to infringe under the "doctrine of equivalents" if "the accused product or process contain[s] elements identical or equivalent to each claimed element of the patented invention." *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 40 (1997).

15. "[A]s between the patentee who had a clear opportunity to negotiate broader claims but did not do so, and the public at large, it is the patentee who must bear the cost of its failure to seek protection for [a] foreseeable alteration of its claimed structure." *Sage Products*, 126 F.3d 1420, 1425 (Fed. Cir. 1997). A patent "contains clear structural limitations," on which "the public has a right to rely … in conducting its business activities." *Id.* The doctrine of equivalents may not be used to "effectively remove" these limitations. *Id*. at 1425-26.

16. The doctrine of equivalents cannot expand the scope of an "about" claim further. *See Cohesive Techs., Inc. v. Waters Corp*., 543 F.3d 1351, 1372 (Fed. Cir. 2008) ("by electing to include the broadening word 'about' in the claim, the patentee has in this case already captured what would otherwise be equivalents within the literal scope of the claim").

17. Prosecution history estoppel "serves to limit the doctrine of equivalents by denying equivalents to a claim limitation whose scope was narrowed during prosecution for reasons related

to patentability." *Pioneer Magnetics, Inc. v. Micro Linear Corp.*, 330 F.3d 1352, 1356 (Fed. Cir. 2003). *See also, Festo Corp v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 734 (2002). *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1366 (Fed. Cir. 2003) (en banc).

18. "[W]hen a patent drafter discloses but declines to claim subject matter, as in this case, this action dedicates that unclaimed subject matter to the public." *Johnson & Johnston Assocs. Inc. v. R.E. Serv. Co*., 285 F.3d 1046, 1054 (Fed. Cir. 2002) "The disclosure-dedication rule requires an inventor who discloses specific matter to claim it, and to submit the broader claim for examination. Otherwise, that matter is dedicated to the public and may not be recaptured under the doctrine of equivalents." *PSC Computer Products, Inc. v. Foxconn Intern., Inc*., 355 F.3d 1353, 1360 (Fed. Cir. 2004). "A patentee may not write narrow claims for allowance by the PTO and subsequently attempt to broaden the claims in court by using the doctrine of equivalents." *Id.* at 1357. "[T]he patentee, rather than the public, must bear the burden of inadvertent errors in the patent—including inadvertent dedications." *Id.* at 1359. "[A]s between the patentee who had a clear opportunity to negotiate broader claims but did not do so, and the public at large, it is the patentee who must bear the cost of its failure to seek protection for [a] foreseeable alteration of its claim structure." *Sage Products, Inc. v. Devon Industries, Inc*., 126 F.3d 1420, 1425 (Fed. Cir. 1997) "[I]ntent is not part of the … disclosure-dedication analysis." *Toro Co. v. White Consolidated Industries, Inc*., 383 F.3d 1326, 1333 (Fed. Cir. 2004)

C. Obviousness

19. A patent issued by the United States Patent and Trademark Office ("PTO") is presumed to be valid. 35 U.S.C. § 282(a). "The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity." *Id*. Invalidity must be established

by facts supported by "clear and convincing evidence." *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 110–14 (2011).

20. However, the presumption of validity is "far from determinative," and a trial court may consider the evidence and decide the issue differently from the PTO. *See AK Steel Corp. v Sollac & Ugine*, 344 F.3d 1234, 1245 (Fed. Cir. 2003); *Purdue Pharma L.P. v. Faulding, Inc.*, 230 F.3d 1320, 1329 (Fed. Cir. 2000).

21. Under 35 U.S.C. § 103(a), a patent may not be obtained "if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains." 35 U.S.C. § 103.

22. Obviousness is a question of law based on four underlying factual inquiries: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art; and (4) secondary considerations of non-obviousness. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406-07, 415 (2007); *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966).

23. Obviousness is determined at the time of invention. 35 U.S.C. § 103. There is a presumption that the date of invention is the filing date of the application. The presumption may be superseded by evidence showing a date of invention prior to the effective date of the reference. *Proctor & Gamble Co. v. Teva Pharm., USA, Inc.*, 566 F.3d 989, 999 (Fed. Cir. 2009).

24. To prove that a claimed invention was obvious at the time it was made, a patent challenger must establish "that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan

would have had a reasonable expectation of success in doing so." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1361 (Fed. Cir. 2007).

25. Obviousness is judged under "an expansive and flexible approach" driven by "common sense." *KSR*, 550 U.S. at 415–18. In *KSR*, the Supreme Court rejected the rigid application of the principle that there should be an explicit teaching, suggestion, or motivation in the prior art in order to find obviousness. *See id*. at 415. "[A]ny need or problem known in the relevant field of endeavor at the time of the invention and addressed by the patent can provide reason for combining the elements in the manner claimed." *KSR*, 550 U.S. at 420. "This includes, but is not limited to, the particular problem the inventors of the patent in question were attempting to solve." *PBI Performance Prods., Inc. v. NorFab Corp*., 514 F. Supp. 2d 732, 742 (E.D. Pa. 2007) (citing *KSR*, 127 S. Ct. 1727, 1742 (2007)). "If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability." *KSR*, 550 U.S. at 417. "When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." *KSR*, 550 U.S. at 421; *see also In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009).

26. "The normal desire of artisans to improve upon what is already generally known can provide the motivation to optimize variables" such as percentages of components for use in known formulations. *In re Ethicon, Inc.*, 844 F.3d 1344, 1351 (Fed. Cir. 2017); *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003) ("a prima facie case of obviousness exists when the claimed range and the prior art range do not overlap but are close enough such that one skilled in the art would have expected them to have the same properties."); *see also In re Boesch*, 617 F.2d 272, 276 (CCPA 1980) ("[D]iscovery of an optimum value of a result effective variable in a known

process is ordinarily within the skill of the art."); *In re Aller*, 220 F.2d 454, 456 (CCPA 1955) ("where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.").

27. This principle is not limited to situations where there is an exact overlap in claimed ranges. *See Pfizer Inc. v. Sanofi Pasteur Inc.*, 94 F.4th 1341, 1348 (Fed. Cir. 2024) ("A routine optimization analysis generally requires consideration whether a person of ordinary skill in the art would have been motivated, with a reasonable expectation of success, to bridge any gaps in the prior art to arrive at a claimed invention. Where that gap includes a parameter not necessarily disclosed in the prior art, it is not improper to consider whether or not it would have been recognized as result-effective. If so, then the optimization of that parameter is 'normally obvious.'" (quoting *In re Antonie*, 559 F.2d 618, 620 (CCPA 1977)).

28. Commercial realities can also drive a motivation to modify the prior art. *DyStar Textilfarben GmbH v. C.H. Patrick Co*., 464 F.3d 1356, 1368 (Fed. Cir. 2006); *see also Dippin' Dots, Inc. v. Mosey*, 476 F.3d 1337, 1344–45 (Fed. Cir. 2007). Where there are few options, simple design choices can suffice to show a motivation to combine. *Asyst Tech., Inc. v. Emtrak, Inc.*, 544 F.3d 1310, 1314-16 (Fed. Cir. 2008) (affirming JMOL of obviousness vacating jury finding of no motivation to combine where the "two alternative means" of achieving the function "have long been known and understood by persons of ordinary skill in the art"); *In re Singhal*, 602 F. App'x 826, 830-31 (Fed. Cir. 2015) (affirming obviousness finding of motivation to combine first reference with second reference in analogous field "as a routine design choice" in part because there were "a finite number—only two—of known and predictable solutions").

29. Moreover, a person of ordinary skill in the art need only be motivated to pursue a suitable option from which the prior art did not teach away, not the best option. *Par Pharm., Inc.*,

v. TWI Pharms. Inc., 773 F.3d 1186, 1197–98 (Fed. Cir. 2014) (citing *Galderma Labs., L.P. v. Tolmar, Inc*., 737 F.3d 731, 738 (Fed. Cir. 2013); *Bayer Healthcare Pharm., Inc. v. Watson Pharm., Inc*., 713 F.3d 1369, 1376 (Fed. Cir. 2013)) ("Our precedent, however, does not require that the motivation be the best option, only that it be a suitable option from which the prior art did not teach away."); *Infineum USA L.P. v. Chevron Oronite Co. LLC*, No. 2020-1333, 2022 WL 3147683, at *6 (Fed. Cir. Aug. 8, 2022) ("We have rejected the notion that a patent challenger seeking to demonstrate obviousness must prove that a person of ordinary skill would have been motivated to select one prior art disclosure over another."). A "disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed. . . ." *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004). A reference does not teach away if it merely expresses a general preference of an alternative invention, but does not criticize, discredit, or otherwise discourage investigation into the invention claims. *Galderma Labs*, 737 F.3d at 738.

30. "Obviousness does not require absolute predictability of success" but rather requires "a reasonable expectation of success." *See Medichem, S.A. v. Rolado, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006) (quoting *In re O'Farrell*, 853 F.2d 894, 903–04 (Fed. Cir. 1988)).

31. When the prior art provides the means of making the invention and predicts the results, and the patentee merely verifies that expectation through "routine testing," the claims are obvious. *Pfizer*, 480 F.3d at 1367; *see also Purdue Pharma Prods. L.P.*, 642 F. Supp. 2d at 370; *Jerry Harvey Audio Holding, LLC v. 1964 Ears, LLC*, 809 F. App'x 919, 923 (Fed. Cir. 2020) ("And if routine experimentation provides for optimizing the phase shift across a frequency range, then we find a motivation to produce a phase corrected response in the claimed frequency range and a reasonable expectation of success in doing so."); *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348,

1368 (Fed. Cir. 2007) ("The experimentation needed, then, to arrive at the subject matter claimed in the '303 patent was nothing more than routine application of a well-known problem-solving strategy, and we conclude, the work of a skilled artisan, not of an inventor.").

32. Objective evidence of non-obviousness includes, inter alia, commercial success, long felt but unsolved needs, surprising and unexpected results and industry praise. *See Graham*, 383 U.S. at 17-18. In determining whether or not claims are obvious, the court weighs secondary considerations, to the extent they exist, with the other parts of the obviousness analysis to determine whether the claims would have been obvious to a person of ordinary skill in the art. *See Alcon Research Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1365-66 (Fed. Cir. 2012). The presence of objective evidence does not mandate a finding of non-obviousness. *See Merck Sharp & Dohme Corp. v. Hospira, Inc.*, 874 F.3d 724, 731 (Fed. Cir. 2017) ("In any event, as with the evidence of commercial success, the district court found that the evidence of copying could not overcome the weight of the competing evidence of obviousness of the claimed process. We agree with the district court. The claimed process differs from the disclosure of the '323 patent only in routine details, the implementation of which would have been well within the capabilities of one of ordinary skill in the art.")

33. Objective evidence must be due to the merits of the claimed invention beyond what was readily available in the prior art. *J.T. Eaton & Co. v. Atlantic Paste & Glue Co*., 106 F.3d 1563, 1571 (Fed. Cir. 1997); *Ormco Corp. v. Align Tech., Inc*., 463 F.3d 1299, 1311-12 (Fed. Cir. 2006); *Novartis AG v. Torrent Pharms. Ltd*., 853 F.3d 1316, 1331 (Fed. Cir. 2017); *In re Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011).

34. "In order to accord substantial weight to secondary considerations in an obviousness analysis, the evidence of secondary considerations must have a 'nexus' to the claims,

i.e., there must be 'a legally and factually sufficient connection' between the evidence and the patented invention." *Fox Factory, Inc. v. SRAM, LLC*, 944 F.3d 1366, 1373 (Fed. Cir. 2019) (citations omitted). "The patentee bears the burden of showing that a nexus exists." *WMS Gaming Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1359 (Fed. Cir. 1999). "To determine whether the patentee has met that burden, we consider the correspondence between the objective evidence and the claim scope." *Henny Penny Corp. v. Frymaster LLC*, 938 F.3d 1324, 1332 (Fed. Cir. 2019).

35. Commercial success of a product that is largely due to name-recognition, marketing, or previous sales, rather than the merits of the invention, provides weak if any evidence of non-obviousness. *Geo M. Martin Co. v. Alliance Mach. Sys. Int'l, LLC*, 618 F.3d 1294, 1304 (Fed. Cir. 2010); *In re DBC*, 545 F.3d 1373, 1384 (Fed. Cir. 2008); *Sandt Tech., Ltd. v. Resco Metal & Plastics Corp.*, 264 F.3d 1344, 1355 (Fed. Cir. 2001); *Pentec, Inc. v. Graphic Controls Corp.*, 776 F.2d 309, 316 (Fed. Cir. 1985); *Bos. Sci. SciMed, Inc. v. Iancu*, 811 F. App'x 618, 628 (Fed. Cir. 2020). Rather, the patentee must show the commercial success was due to the allegedly novel features over the prior art. *Tokai Corp. v. Easton Enterprises, Inc.*, 632 F.3d 1358, 1370 (Fed. Cir. 2011)

36. Evidence of a longfelt need for the invention must also show that the need was not met prior to the invention. *Geo M. Martin Co. v. Alliance Mach. Sys. Int'l, LLC*, 618 F.3d 1294, 1304 (Fed. Cir. 2010). Further, long-felt need is not probative of obviousness if not filling the need was due to business-driven decisions rather than technical inadequacy. *Friskit, Inc. v. Real Networks, Inc.*, 306 F. App'x 610, 617-18 (Fed. Cir. 2009); *Orthopedic Equip. Co., Inc. v. U.S.*, 702 F.2d 1005, 1013 (Fed. Cir. 1983); *Adapt Pharma Operations Ltd. v. Teva Pharm. USA, Inc.*, 25 F.4th 1354, 1376 (Fed. Cir. 2022).

37. Evidence of failure of others does not show non-obviousness when such failures are unrelated to the merits of the claimed invention. *Boston Sci. Scimed, Inc. v. Cordis Corp.*, 554 F.3d 982, 991-92 (Fed. Cir. 2009); *George M. Martin Co. v. All. Mach. Sys. Int'l LLC*, 618 F.3d 1294 (Fed. Cir. 2010).

38. Evidence of skepticism must go to the likely success of a combination or solution. *WBIP, LLC v. Kohler Co*., 829 F.3d 1317, 1335-36 (Fed. Cir. 2016); *Neptune Generics v. Eli Lilly and Co.*, 921 F.3d 1372, 1378 (Fed. Cir. 2019); *AstraZeneca LP v. Breath Ltd*., 603 F. App'x 999, 1003-04 (Fed. Cir. 2015); *In re Magna Elecs., Inc*., 611 F. App'x 969, 973 (Fed. Cir. 2015).

39. In the pharmaceutical context, evidence of copying does not support nonobviousness. *Bayer Healthcare Pharm., Inc. v. Watson Pharm., Inc*., 713 F.3d 1369, 1377 (Fed. Cir. 2013).

40. Evidence of independently made, simultaneous inventions is a secondary consideration supporting obviousness. *George M. Martin Co. v. Alliance Mach. Sys. Int'l LLC*, 618 F.3d 1294, 1305 (Fed. Cir. 2010) ("Independently made, simultaneous inventions, made within a comparatively short space of time, are persuasive evidence that the claimed apparatus was the product only of ordinary mechanical or engineering skill.").

D. Written Description

41. "35 U.S.C. § 112, first paragraph, requires a 'written description of the invention' which is separate and distinct from the enablement requirement." *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). "The purpose of the 'written description' requirement is broader than to merely explain how to 'make and use'; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of

the invention." *Id*. "The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." *Id.* at 1564 (emphasis in original).

42. When an applicant claims a specific result, that result must be adequately supported in the specification. *Nuvo Pharms. (Ireland) Designated Activity Co. v. Dr. Reddy's Lab'ys Inc.*, 923 F.3d 1368 (Fed. Cir. 2019) ("In light of the fact that the specification provides nothing more than the mere claim that uncoated PPI might work, even though persons of ordinary skill in the art would not have thought it would work, the specification is fatally flawed. It does not demonstrate that the inventor possessed more than a mere wish or hope that uncoated PPI would work, and thus it does not demonstrate that he actually invented what he claimed."). "Although inventor testimony cannot establish written description support where none exists in the four corners of the specification, it" may "illuminate[] the absence of critical description." *Id.*

E. Enablement

43. The enablement requirement asks whether "the specification teach[es] those in the art to make and use the invention without undue experimentation." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). To satisfy this requirement, "[t]he specification must contain sufficient disclosure to enable an ordinarily skilled artisan to make and use the entire scope of the claimed invention at the time of filing." *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1381 (Fed. Cir. 2012).

44. "To prove that a claim is invalid for lack of enablement, a challenger must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation.'" *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014) (quoting *In re Wands*, 858 F.2d at 736-37). In analyzing undue experimentation, we consider factors such as: "(1) the quantity of experimentation

necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *In re Wands*, 858 F.2d at 737.

45. The "specification must enable the full scope of the claimed invention." *Trustees of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1364 (Fed. Cir. 2018). Where certain permutations are impossible, the claims are invalid as a matter of law for lack of enablement. *See id.* ("BU notes that there is no dispute as to enablement of five out of the six referenced permutations and argues '[t]hat is sufficient.'…We disagree.")

II. THE ASSERTED CLAIMS ARE NOT INFRINGED

46. Ingenus will not be able to prove that Accord's ANDA product infringes any claim of the 952 patent, specifically that Accord's ANDA product contains "an ethanol content of about 70% to about 70% 75%" (claim 1) "cyclophosphamide in a concentration of about 23%" and "an ethanol content of about 70%" (claim 4). Accord's ANDA product contains 68.74% ethanol and 22.17% cyclophosphamide which are not within the literal scope of the claims to the extent they can be construed.

47. Ingenus cannot resort to infringement under the doctrine of equivalents because (1) DOE is not available to further expand the scope of "about" claims; (2) the doctrines of prosecution history estoppel and the disclosure-dedication rule bar resort to equivalents. Specifically, the specification discloses broader ranges, but the applicants surrendered such scope for reasons related to patentability.

III. THE ASSERTED CLAIMS ARE INVALID FOR OBVIOUSNESS

48. The asserted claims are invalid under 35 U.S.C. § 103 because the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains.

IV. THE ASSERTED CLAIMS ARE INVALID FOR LACK OF WRITTEN DESCRIPTION AND ENABLEMENT UNDER 35 U.S.C. §112

49. The asserted claims are invalid under 35 U.S.C. § 112 because the specification does not show the inventors were in possession of the full scope of the claims or enabled a person of skill in the art to carry out the full scope of the claims.

EXHIBIT 6

UNREDACTED PUBLIC VERSION

Ingenus Pharmaceuticals, LLC, and Leiutis Pharmaceuticals LLP v. Accord Healthcare, Inc.
23-cv-377-JLH

Trial Dates: March 24-27, 2025

JOINT EXHIBIT LIST

JTX No.	Description	(PTX No.)
1	United States Patent No. 10,993,952	PTX-129
2	File History for United States Patent No. 10,993,952	PTX-080
3	United States Patent No. 4,879,286 (Alam)	PTX-138
4	United States Patent Application Publication No. 2015/0320775 (Palepu)	PTX-140
5	WO 2016/005962 (Shaik)	PTX-137
6	United States Patent No. 4,952,575 (Sauerbier)	PTX-139
7	WO 02/02125 (Tait)	PTX-136
8	FDA Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products	PTX-143
9	B. Nagaraju Declaration 10-1-19	PTX-084
10	B. Nagaraju Declaration 4-8-20	PTX-082
11	Chandrashekar Declaration 10-1-19	PTX-085
12	Chandrashekar Declaration 4-8-20	PTX-083
13	Chandrashekar Declaration 1-14-21	PTX-081
14	Accord ANDA Section 3.2.P.1	PTX-007
15	S. Pramanick, et al., "Excipient Selection in Parenteral Formulation Development," Pharma Times, Vol. 45 No. 3, 65-77 (March, 2013)	PTX-157
16	Ingenus label	Zamboni ¶

EXHIBIT 7

UNREDACTED PUBLIC VERSION

Ingenus Pharmaceuticals, LLC, and Leiutis Pharmaceuticals LLP v. Accord Healthcare, Inc.,
23-cv-377-JLH
PLAINTIFFS' EXHIBIT LIST

PTX No.	Description	Bates Start	Bates End	Defendant's Objections
PTX-001	draft prescribing information	ACC-CYC0000049	ACC-CYC0000068	
PTX-002	Controlled Correspondence 19953 Q1/Q2 Formulation Assessment for Cyclophosphamide Injection 500 mg/2.5 ml	ACC-CYC0000093	ACC-CYC0000113	
PTX-003	draft-labeling-text-word.docx	ACC-CYC0000156	ACC-CYC0000173	
PTX-004	1.2.15 Request for Waiver, Cyclophosphamide Injection 200 mg/ml	ACC-CYC0000217	ACC-CYC0000217	
PTX-005	1.4.2 Statement of right of references	ACC-CYC0000279	ACC-CYC0000287	
PTX-006	2.3.P DRUG PRODUCT	ACC-CYC0000305	ACC-CYC0000388	
PTX-007	3.2.P.1 DESCRIPTION AND COMPOSITION OF DRUG PRODUCT	ACC-CYC0000530	ACC-CYC0000532	
PTX-008	3.2.P.2 PHARMACEUTICAL DEVELOPMENT	ACC-CYC0000533	ACC-CYC0000551	
PTX-009	Manufacturing Process Development	ACC-CYC0000552	ACC-CYC0000602	
PTX-010	Dilution Study	ACC-CYC0000652	ACC-CYC0000740	
PTX-011	process-validation-dry-heat-sterilizer	ACC-CYC0001197	ACC-CYC0001303	
PTX-012	Bubble point ratio determination study	ACC-CYC0001304	ACC-CYC0001399	
PTX-013	Isolator recent periodic validation	ACC-CYC0001400	ACC-CYC0001508	
PTX-014	process validation - media fill	ACC-CYC0001515	ACC-CYC0001586	
PTX-015	3.2.P.3.5 Process Validation and / or Evaluation	ACC-CYC0001587	ACC-CYC0001617	
PTX-016	Process validation document - Cyclophosphamide Injection 200 mg/mL, 10 mL	ACC-CYC0001618	ACC-CYC0001802	
PTX-017	3.2.P.4.2 Analytical Procedure [Dehydrated Alcohol]	ACC-CYC0001803	ACC-CYC0001810	
PTX-018	3.2.P.4.4 Justification of Specifications [Dehydrated alcohol]	ACC-CYC0001811	ACC-CYC0001820	
PTX-019	3.2.P.4.1 Specifications [Dehydrated Alcohol]	ACC-CYC0001821	ACC-CYC0001827	
PTX-020	3.2.P.4.2 Analytical Procedure [Monothioglycerol]	ACC-CYC0001830	ACC-CYC0001834	
PTX-021	3.2.P.4.4 Justification of Specifications [Monothioglycerol]	ACC-CYC0001835	ACC-CYC0001842	
PTX-022	3.2.P.4.1 Specifications [Monothioglycerol]	ACC-CYC0001843	ACC-CYC0001846	
PTX-023	3.2.P.4.4 Justification of Specifications [Nitrogen Gas]	ACC-CYC0001852	ACC-CYC0001862	
PTX-024	3.2.P.4.1 Specifications [Nitrogen Gas]	ACC-CYC0001863	ACC-CYC0001870	
PTX-025	3.2.P.4.2 Analytical Procedure [Propylene Glycol]	ACC-CYC0001873	ACC-CYC0001882	
PTX-026	3.2.P.4.4 Justification of Specifications [Propylene Glycol]	ACC-CYC0001883	ACC-CYC0001889	
PTX-027	3.2.P.4.1 Specifications [Propylene glycol]	ACC-CYC0001890	ACC-CYC0001896	
PTX-028	3.2.P.4.3 Validation of Analytical Procedure [Propylene Glycol]	ACC-CYC0001897	ACC-CYC0001926	
PTX-029	3.2.P.4.2 Analytical Procedure [Macrogol 400 (Polyethylene glycol)]	ACC-CYC0001927	ACC-CYC0001936	
PTX-030	3.2.P.4.4 Justification of Specifications [Macrogol 400 (Polyethylene glycol)]	ACC-CYC0001937	ACC-CYC0001944	
PTX-031	3.2.P.4.1 Specifications [Macrogol 400 (Polyethylene glycol)]	ACC-CYC0001945	ACC-CYC0001953	
PTX-032	3.2.P.4.3 Validation of Analytical Procedure [Macrogol 400 (Polyethylene glycol)]	ACC-CYC0001954	ACC-CYC0001998	
PTX-033	3.2.P.5 CONTROL OF DRUG PRODUCT (3.2.P.5.1 Specification(s))	ACC-CYC0001999	ACC-CYC0002024	
PTX-034	3.2.P.5.2 Analytical Procedure	ACC-CYC0002025	ACC-CYC0002040	
PTX-035	3.2.P.5.3 Validation of Analytical Procedure	ACC-CYC0002041	ACC-CYC0002042	
PTX-036	Validation - Analytical method transfer	ACC-CYC0002043	ACC-CYC0002116	
PTX-037	Method validation for identification by UV-Visible spectrophotometer	ACC-CYC0002117	ACC-CYC0002700	

PTX-038	3.2.P.5.4 Batch Analysis	ACC-CYC0002701	ACC-CYC0002880	
PTX-039	3.2.P.5.5 Characterization of Impurities	ACC-CYC0002881	ACC-CYC0002916	
PTX-040	3.2.P.5.6 Justification of Specification	ACC-CYC0002917	ACC-CYC0002992	
PTX-041	container closure system extractables study	ACC-CYC0003200	ACC-CYC0003423	
PTX-042	3.2.P.8.3 Stability Data	ACC-CYC0003427	ACC-CYC0003483	
PTX-043	Cyclophosphamide Injection 200 mg/mL (2.5 mL) - Long term Stability Data	ACC-CYC0003484	ACC-CYC0003557	
PTX-044	Cyclophosphamide Injection 200 mg/mL, 5mL Batch - M2205759	ACC-CYC0003562	ACC-CYC0004662	
PTX-045	Cyclophosphamide Injection 200 mg/mL, 10\mL Batch - M2205654	ACC-CYC0004663	ACC-CYC0005866	
PTX-046	Cyclophosphamide Injection 200 mg/mL, 2.5mL Batch - M2205755	ACC-CYC0005867	ACC-CYC0007048	
PTX-047	Cyclophosphamide Injection 200 mg/mL Common Bulk	ACC-CYC0007049	ACC-CYC0007227	
PTX-048	3.2.R REGIONAL INFORMATION (3.2.R.P Drug Product)	ACC-CYC0007228	ACC-CYC0007236	
PTX-049	ACCORD ANDA	ACC-CYC0007237	ACC-CYC0007240	
PTX-050	ACCORD ANDA	ACC-CYC0007279	ACC-CYC0007331	
PTX-051	ACCORD ANDA	ACC-CYC0007332	ACC-CYC0007391	
PTX-052	ACCORD ANDA	ACC-CYC0007392	ACC-CYC0007701	
PTX-053	ACCORD ANDA	ACC-CYC0007702	ACC-CYC0007777	
PTX-054	ACCORD ANDA	ACC-CYC0007983	ACC-CYC0008000	
PTX-055	ACCORD ANDA	ACC-CYC0008279	ACC-CYC0008304	
PTX-056	ACCORD ANDA	ACC-CYC0008433	ACC-CYC0008433	
PTX-057	ACCORD ANDA	ACC-CYC0008491	ACC-CYC0008497	
PTX-058	ACCORD ANDA	ACC-CYC0008506	ACC-CYC0008506	
PTX-059	Discipline Review Letter (Labeling) dated July 25, 2023 Response	ACC-CYC0008545	ACC-CYC0008551	
PTX-060	Accord Patent Certification for patent in suit	ACC-CYC0008605	ACC-CYC0008606	
PTX-061	FDA-Communication [Complete Response]-000x-	ACC-CYC0009895	ACC-CYC0009900	
PTX-062	Flexible sponge electrode structure for cathode of metal-air battery comprising a membrane in which fibrillated fibers form a network By: Lee, Jung-Ho; Shinde, Sambhaji Shivaji; Kim, Dong-Hyung	ACC-CYC0022873	ACC-CYC0022914	401/402, Hearsay
PTX-063	Flexible sponge electrode structure for cathode of metal-air battery comprising a membrane in which fibrillated fibers form a network By: Lee, Jung-Ho; Shinde, Sambhaji Shivaji; Kim, Dong-Hyung	ACC-CYC0022924	ACC-CYC0022982	401/402, Hearsay
PTX-064	Flexible sponge electrode structure for cathode of metal-air battery comprising a membrane in which fibrillated fibers form a network By: Lee, Jung-Ho; Shinde, Sambhaji Shivaji; Kim, Dong-Hyung	ACC-CYC0022983	ACC-CYC0023047	401/402, Hearsay
PTX-065	Combinations of drugs with antisense oligonucleotides for treatment of proliferative diseases By: Muller, Marcel; Geiger, Thomas; Altmann, Karl-Heinz; Fabbro, Doriano; Dean, Nicholas Mark; Monia, Brett; Bennett, Clarence Frank	ACC-CYC0023484	ACC-CYC0023519	401/402, Hearsay
PTX-066	Method for determining treatment efficacy in B-cell chronic lymphocytic leukaemia By: Chuksina, Yu. Yu.; Yazdovskii, V. V.; Moskalets, O. V.; Shevelev, S. V.; Kataeva, E. V.; Golenkov, A. K.	ACC-CYC0023656	ACC-CYC0023793	401/402, Hearsay

PTX-067	Preparation of prodrugs for enzyme-mediated activation By: Bosslet, Klaus; Czec, Joerg; Hoffmann, Dieter; Tillequin, Francois; Florent, Jean-Claude; Azoulay, Michel; Monneret, Claude; Jacquesy, Jean-Claude; Gesson, Jean-Pierre; Et, Al.	ACCCYC0023932	ACCCYC0024020	401/402, Hearsay
PTX-068	Accord Notice Letter Cyclophosphamide RTU_2023-02-20	ACC-CYC0024696	ACC-CYC0024705	
PTX-069	Liposome compositions for cancer therapy, and manufacture thereof By: Aoki, Yoichi; Ueda, Eiichi	ACC-CYC0029066	ACC-CYC0029090	401/402, Hearsay
PTX-070	NEWPORT Report Cyclophosphamide	ACC-CYC0030654	ACC-CYC0030654	401/402, Hearsay
PTX-071	Email chain. Top email from Kuldeep Karnik to Alpesh Pathak	ACC-CYC0030708	ACC-CYC0030711	
PTX-072	Email chain. Top email from Manan Shroff to Alpesh Pathak	ACC-CYC0030733	ACC-CYC0030736	
PTX-073	3.2.P.1 DESCRIPTION AND COMPOSITION OF THE DRUG PRODUCT	ACC-CYC0033287	ACC-CYC0033287	
PTX-074	A218250_Quality_DRL	ACC-CYC0033323	ACC-CYC0033330	
PTX-075	Email chain. Top email from Dhaval Dadhaniya to Rahul Talekar	ACC-CYC0035150	ACC-CYC0035151	
PTX-076	Email chain. Top email from Rajesh Baldha to Jaimin Gandhi	ACC-CYC0036600	ACC-CYC0036602	
PTX-077	3.2.P.1 DESCRIPTION AND COMPOSITION OF THE DRUG PRODUCT	ACC-CYC0036605	ACC-CYC0036606	
PTX-078	Cyclophosphamide Injection, 200 mg/ml, DCP - Day 70 RMS Comments	ACC-CYC0036607	ACC-CYC0036608	
PTX-079	Email from Alpesh Pathak to Nimish Chudgar	ACC-CYC0045022	ACC-CYC0045022	
PTX-080	File History	ING000000001	ING000000628	
PTX-081	DECLARATION UNDER 37 CFR §1.132	ING00000085	ING00000089	
PTX-082	DECLARATION UNDER 37 CFR §1.132	ING00000146	ING00000150	
PTX-083	DECLARATION UNDER 37 CFR §1.132	ING00000151	ING00000155	
PTX-084	DECLARATION UNDER 37 CFR §1.132	ING00000231	ING00000238	
PTX-085	DECLARATION UNDER 37 CFR §1.132	ING00000239	ING00000246	
PTX-086	2.3.P DRUG PRODUCT	ING00001378	ING00001475	
PTX-087	LPPDNB-201	LEI00000686	LEI00000828	401/402, Foundation, Hearsay
PTX-088	LPPDNB-237	LEI00000829	LEI00000888	401/402, Foundation, Hearsay
PTX-089	LPPDNB-201 Annexures	LEI00001110	LEI00001123	401/402, Foundation, Hearsay
PTX-090	LPPDNB-237 Annexures	LEI00001124	LEI00001131	401/402, Foundation, Hearsay
PTX-091	Plaintiffs' Rule 26(a) Initial Disclosures			401/402, Hearsay
PTX-092	Defendant's Initial Disclosures Pursuant to FRCP 26(a)(1)			
PTX-093	Plaintiffs' Preliminary Disclosure of Asserted Claims			401/402, Hearsay
PTX-094	Defendant's Initial Invalidity and Noninfringement Contentions			
PTX-095	Prior Art Sent With Invalidity Contentions			
PTX-096	Plaintiffs' Initial Infringement Contentions with Exhibit A			401/402, Hearsay
PTX-097	Defendant's First Set of Interrogatories (Nos. 1-6)			401/402, Hearsay

PTX-098	Defendant's First Set of RFPs			401/402, Hearsay
PTX-099	Plaintiffs' First Set of Interrogatories (Nos. 1-11)			401/402, Hearsay
PTX-100	Plaintiffs' First Set of RFPs			401/402, Hearsay
PTX-101	Plaintiffs' Response to Defendant's First Set of Interrogatories (Nos. 1-6)			401/402, Hearsay
PTX-102	Plaintiffs' Responses to Defendant's First Set of RFPs			401/402, Hearsay
PTX-103	Defendant's Response to Plaintiffs' First Set of Interrogatories (Nos. 1-11)			
PTX-104	Defendant's Response to Plaintiffs' First Set of RFPs			
PTX-105	Plaintiffs' Claim construction Issue Identification			401/402, Hearsay
PTX-106	Defendant's First Set of RFAs			401/402, Hearsay
PTX-107	Defendant's Second Set of Interrogatories (Nos. 7-13)			401/402, Hearsay
PTX-108	Plaintiffs' First Set of RFAs			401/402, Hearsay
PTX-109	Plaintiffs' Second Set of Interrogatories (Nos. 12-20)			401/402, Hearsay
PTX-110	Defendant's Responses to Plaintiffs' First Request for Admissions (Nos. 1-68)			
PTX-111	Plaintiffs' Responses to Defendant's First Set of RFAs			401/402, Hearsay
PTX-112	Plaintiffs' Responses to Defendant's Second Set of Interrogatories (Nos. 7-13)			401/402, Hearsay
PTX-113	Defendant's Response to Plaintiffs' Second Set of Interrogatories (Nos. 12-20)			
PTX-114	Accord's Amended Invalidity and Noninfringement Contentions dated June 6, 2024			
PTX-115	Plaintiffs' Supplemental Response to Accord's First & Second Rogs (1-13)			401/402, Hearsay
PTX-116	Defendant's Responses and Objections to Plaintiffs' Notice of Deposition of Accord Healthcare, Inc. Pursuant to FRCP 30(b)(6)			
PTX-117	First Supplemental Responses to Plaintiffs' Second Set of ROGS (Nos. 12-20)			
PTX-118	Defendant's Supplemental Responses to Plaintiffs' First Requests for Admission dated July 29, 2024			
PTX-119	Supplemental Responses to Plaintiffs 1st Requests for Admission (1-68)			
PTX-120	Opening Expert Report of Jason McConville			401/402, Hearsay
PTX-121	McConville Reply Report			401/402, Hearsay
PTX-122	Yaman Reply Expert Report - Infringement			401/402, Hearsay
PTX-123	McConville Responsive Expert Report			401/402, Hearsay
PTX-124	Yaman Expert Report - Infringement			401/402, Hearsay
PTX-125	Yaman Validity Expert Report			401/402, Hearsay
PTX-126	Zamboni Expert Report			401/402, Hearsay
PTX-127	DECLARATION UNDER 37 CFR §1.132			
PTX-128	Notice of Allowability			
PTX-129	U.S. Patent No. 10,993,952			
PTX-130	Complaint for Patent Infringement			401/402, Hearsay
PTX-131	~~Shaik Indian Provisional Application '3454~~ Reserved			
PTX-132	~~Shaik Indian Provisional Application '3454~~ Reserved			
PTX-133	US 2005/0272698 A1 (Daftary)			
PTX-134	US 2014/0005148 A1 (Neelakantan)			

PTX-135	~~US Provisional Patent App 61/991,247 Palepu~~ Reserved			
PTX-136	International Publication Number WO 02/02125 (Tait)			
PTX-137	International Publication Number WO 2016/005962 A2 (Shaik)			
PTX-138	U.S. Patent No. 4,879,286, Alam et al.			
PTX-139	U.S. Patent No. 4,952,575, Sauerbier et al.			
PTX-140	United States Patent Application Publication Number 2015/0320775, Palepu et al.			
PTX-141	~~Auromedics FDA Approval Letter~~ Reserved			
PTX-142	~~Auromedics label~~ Reserved			
PTX-143	FDA Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products (November 2003)			
PTX-144	Linkedin profile, K Chandrashekhar			401/402, Hearsay
PTX-145	A. Jayagopal and V. Prasad Shastri, “Nanoengineering of drug delivery systems” ch. 7 in Nanoparticulate Drug Delivery Systems ed. D. Thassu, M. Deleers and Y. Pathak, Informa Healthcare, New York, 2007. P. 106			401/402, Hearsay, Not Produced
PTX-146	B.E. Rabinow. Nanosuspensions in Drug Delivery, Nature Reviews Drug Discovery 3:785-796 (2004)			401/402, Hearsay, Not Produced
PTX-147	Cayman Chemical data sheets for cyclophosphamide and ifosfamide			401/402, Hearsay, Not Produced
PTX-148	Cyclophosphamide Injection Product Information from Eugia website			
PTX-149	Cyclophosphamide RTU US scenario			
PTX-150	Excerpt from file history 18/547,260 (Declaration for Utility of Design Application Using an Application Data Sheet)			401/402, Hearsay, Not Produced
PTX-151	Kennedy R, Groepper D, Tagen M, et al. Stability of Cyclophosphamide in Extemporaneous Oral Suspensions, Annals of Pharmacotherapy, 2010;44(2):295-301			401/402, Hearsay, Not Produced
PTX-152	Lee SE, Bairstow SF, Werling JO, Chaubal MV, Lin L, Murphy MA, DiOrio JP, Gass J, Rabinow B, Wang X, Zhang Y, Yang Z, Hoffman RM. Paclitaxel nanosuspensions for targeted chemotherapy – nanosuspension preparation, characterization, and use. Pharm Dev Technol. 2013 Jun; 19(4):438-53			401/402, Hearsay, Not Produced
PTX-153	LinkedIn profile, Ajeet Singh			
PTX-154	LinkedIn profile, Karnik Kuldeep			
PTX-155	Nyhammar, E. and Eksborg, S.(1991)'Correspondence and Short Communications: Dissolution Time for Three Formulations of Cyclophosphamide Powder for Injection', Acta Oncologica,30:7,867			401/402, Hearsay, Not Produced
PTX-156	Press Release, Fresenius Kabi Further Expands Oncology Portfolio With Launch of Cyclophosphamide for Injection, USP			401/402, Hearsay, Not Produced
PTX-157	S. Pramanick, et al., “Excipient Selection in Parenteral Formulation Development,” Pharma Times, Vol. 45 No. 3, 65-77 (March, 2013)			
PTX-158	Triclinic Labs Report			401/402, Hearsay, Not Produced

PTX-159	United States Patent Application Publication 2022/0233631 A1 (George)			401/402, Hearsay, Not Produced
PTX-160	US 2024/0139108 Al Bhavsar et al)			401/402, Hearsay, Not Produced
PTX-161	USP (2007)			401/402, Hearsay, Not Produced
PTX-162	Billstein-Leber M, Carrillo CJD, Cassano AT, Moline K, Robertson JJ. ASHP guidelines on preventing medication errors in hospitals. Am J Health Syst Pharm. 2018;75(19):1493–517.			401/402, Hearsay, Not Produced
PTX-163	CDC Alcohol Use (www.cdc.gov/alcohol/standard-drink-sizes/index.html). (May 2024).			401/402, Hearsay, Not Produced
PTX-164	CDC and NIOSH Hazardous Drug Exposures in Healthcare (www.cdc.gov/niosh/healthcare/hazardous-drugs/?CDC_AAref_Val=https://www.cdc.gov/niosh/topics/hazdrug). (March 2024)			401/402, Hearsay, Not Produced
PTX-165	CDC Cancer Data and Statistics (www.cdc.gov/cancer/data/index.html#) (June 2024)			401/402, Hearsay, Not Produced
PTX-166	Chadha P, Gerber PA, Hilton S, Molina B, Haq S, Partridge J, Wong V, Hoffmann K, Persson C, Prygova I. Ready-to-use abobotulinumtoxinA solution versus powder botulinumtoxinA for treatment of glabellar lines: Investigators' and subjects' experience in a Phase IV study. J Cosmet Dermatol. 2024 Sep;23(9):2857-2866.			401/402, Hearsay, Not Produced
PTX-167	Chew L. et. al. Pharmacy Requirements for a Comprehensive Cancer Center. 2021 Oct 29. In: Aljurf M, Majhail NS, Koh MBC, et al., editors. The Comprehensive Cancer Center: Development, Integration, and Implementation [Internet]. Cham (CH): Springer; 2022. Chapter 9.			401/402, Hearsay, Not Produced
PTX-168	Ciccarello C, Leber MB, Leonard MC, et al. ASHP Guidelines on the Pharmacy and Therapeutics Committee and the Formulary System. Am J Health Syst Pharm. 2021 May 6;78(10):907-918.			401/402, Hearsay, Not Produced
PTX-169	Cox J, Speed V, O'Neal S, Hasselwander T, Sherwood C, Eckel SF, Zamboni WC. Development and evaluation of a novel product to remove surface contamination of hazardous drugs. J Oncol Pharm Pract. 2017 Mar;23(2):103-115.			401/402, Hearsay, Not Produced
PTX-170	Cyclophosphamide Injection, Solution, Ingenus Pharmaceuticals, LLC, Package Insert. (Revised 01/2023).			401/402, Hearsay, Not Produced
PTX-171	Cyclophosphamide Injection, Lyophilized Powder Package Insert. (Ref ID 3304966; Revised 05/2013).			401/402, Hearsay, Not Produced
PTX-172	Cyclophosphamide Injection, Eugia US, LLC, Package Insert. (Revised 12/2023).			401/402, Hearsay, Not Produced
PTX-173	Cuesta Esteve I, Fernández P, López Palacios S, Menor Rodríguez MJ, Parra Vino H, Reyero Ortega B, Nieto Nevot ML, Drago Manchón G, López-Belmonte JL. Health care professionals' preference for a fully liquid, ready-to-use hexavalent vaccine in Spain. Prev Med Rep. 2021 Apr 16;22:101376.			401/402, Hearsay, Not Produced

PTX-174	Doessegger L, Mahler HC, Szczesny P, et al. The potential clinical relevance of visible particles in parenteral drugs. J Pharm Sci. 2012 Aug;101(8):2635-44.			401/402, Hearsay, Not Produced
PTX-175	Eskander J, Cotte J, Glenn E, Friedman S, Rosinia F. The incidence of coring and fragmentation of medication vial rubber stoppers. J Clin Anesth. 2015 Aug;27(5):442-4.			401/402, Hearsay, Not Produced
PTX-176	Fanikos J, Erickson A, Munz KE, Sanborn MD, Ludwig BC, Van Hassel T. Observations on the use of ready-to-use and point-of-care activated parenteral products in automated dispensing cabinets in U.S. hospitals. Am J Health Syst Pharm. 2007 Oct 1;64(19):2037-43.			401/402, Hearsay, Not Produced
PTX-177	FDA Inspection of Injectable Products for Visible Particulates Guidance for Industry 2021.			401/402, Hearsay, Not Produced
PTX-178	Gabay M, et al. Third consensus development conference on the safety of intravenous drug delivery systems. Am J Health-Syst Pharmacy. 2020;77(3):215–20.			401/402, Hearsay, Not Produced
PTX-179	Goldspiel B, Hoffman JM, Griffith NL, et al. ASHP guidelines on preventing medication errors with chemotherapy and biotherapy. Am J Health-Syst Pharm. 2015; 72:e6–35.			401/402, Hearsay, Not Produced
PTX-180	Hertig JB, Degnan DD, Scott CR, Lenz JR, Li X, Anderson CM. A comparison of error rates between intravenous push methods: a prospective, multisite, observational study. J Patient Saf. 2018;14(1):60–5.			401/402, Hearsay, Not Produced
PTX-181	Jorgenson JA, et. al., Contamination comparison of transfer devices intended for handling hazardous drugs. Hosp Pharm. 2008;43:723-27.			401/402, Hearsay, Not Produced
PTX-182	Kordi R, White BF, Kennedy DJ. Possibility and Risk of Medication Vial Coring in Interventional Spine Procedures. PM R. 2017 Mar;9(3):289-293. doi: 10.1016/j.pmrj.2016.09.003.			401/402, Hearsay, Not Produced
PTX-183	Lahue BJ, Pyenson B, Iwasaki K, Blumen HE, Forray S, Rothschild JM. National burden of preventable adverse drug events associated with inpatient injectable medications: healthcare and medical professional liability costs. Am Health Drug Benefits. 2012;5(7):1–10.			401/402, Hearsay, Not Produced
PTX-184	Larmené-Beld KHM, Spronk JT-, Luttjeboer J, Taxis K, Postma MJ. A cost minimization analysis of ready-to-administer prefilled sterilized syringes in a Dutch hospital. Clin Ther. 2019;41(6):1139–50.			401/402, Hearsay, Not Produced
PTX-185	Massoomi F. Assessing vial transfer devices for handling hazardous drugs. Pharmacy Purchasing & Products – Hazardous Drugs. 2009;March:18-22.			401/402, Hearsay, Not Produced
PTX-186	Mercaldi CJ, Lanes S, and Bradt J. Comparative risk of bloodstream infection in hospitalized patients receiving intravenous medication by open, point-of-care, or closed delivery systems. Am J Health-Syst Pharm. 2013;70:957-965.			401/402, Hearsay, Not Produced
PTX-187	Parshuram CS, To T, Seto W, Trope A, Koren G, Laupacis A. Systematic evaluation of errors occurring during the preparation of intravenous medication. CMAJ. 2008;178(1):42–8.			401/402, Hearsay, Not Produced
PTX-188	Power LA, Coyne JW. ASHP Guidelines on Handling Hazardous Drugs. Am J Health Syst Pharm. 2018 Dec 15;75(24):1996-2031.			401/402, Hearsay, Not Produced
PTX-189	Procytox Product Monograph 2012.			401/402, Hearsay, Not Produced

PTX-190	Punke AP and Waddell JA. Creation and evaluation of a cancer chemotherapy order review guide for use at a community hospital. J Oncol Pharm Practice 2019;25(1);25–43.			401/402, Hearsay, Not Produced
PTX-191	Salch SA, Zamboni WC, Zamboni BA, Eckel SF. Patterns and characteristics associated with surface contamination of hazardous drugs in hospital pharmacies. Am J Health Syst Pharm. 2019 Apr 17;76(9):591-598.			401/402, Hearsay, Not Produced
PTX-192	Shaikh H, et.al. Formulation options for cyclophosphamide. Pharmacy Purchasing & Products. Oncology Safety 2022;9(2):4.			401/402, Hearsay, Not Produced
PTX-193	Slaughter A. Safe HD handling in an outpatient infusion center. Pharmacy Purchasing & Products. Hazardous Drug 2019;16(6)"18-22.			401/402, Hearsay, Not Produced
PTX-194	Sudhakar S, Jacob A, Hegde NN, Chaudhary RK, Mateti UV, Shetty V. Evaluation of chemotherapy infusion and phlebitis among cancer patients: A prospective observational single-center study. J Oncol Pharm Pract. 2023 Dec;29(8):1944-1950.			401/402, Hearsay, Not Produced
PTX-195	Taxis K, Barber N. Incidence and severity of intravenous drug errors in a German hospital. Eur J Clin Pharmacol. 2004;59(11):815–7.			401/402, Hearsay, Not Produced
PTX-196	USP 800: Hazardous Drugs – Handling in Healthcare Settings (www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare#)			401/402, Hearsay, Not Produced
PTX-197	Van der Linden P, Douschamps J, Schmitt C, and Forget D. Ready-to-Use Injection Preparations versus Conventional Reconstituted Admixtures: Economic Evaluation in a Real-Life Setting. PharmacoEconomics 20(8):529-36.			401/402, Hearsay, Not Produced
PTX-198	www.oncolink.org/cancer-treatment/oncolink-rx/cyclophosphamide-iv-formulation-cytoxan-r-neosar-r-endoxan-r;			401/402, Hearsay, Not Produced
PTX-199	Zamboni WC, Charlab R, Burckart GJ, Stewart CF. Effect of Obesity on the Pharmacokinetics and Pharmacodynamics of Anticancer Agents. J Clin Pharmacol. 2023 Nov;63 Suppl 2:S85-S102.			401/402, Hearsay, Not Produced
PTX-200	US Patent 5,036,060			401/402, Hearsay, Not Produced
PTX-201	US Patent 5,047,246			401/402, Hearsay, Not Produced
PTX-202	US Patent 5,227,374			401/402, Hearsay, Not Produced
PTX-203	NDA 012141			401/402, Hearsay, Not Produced
PTX-204	NDA 012142			401/402, Hearsay, Not Produced
PTX-205	Supplement 107 to NDA 012142			401/402, Hearsay, Not Produced
PTX-206	FI 87526B			401/402, Hearsay, Not Produced
PTX-207	U.S. Patent Application Publication No. 2015/0290226			401/402, Hearsay, Not Produced

PTX-208	U.S. Patent Application Publication No. 2018/0104264			401/402, Hearsay, Not Produced
PTX-209	U.S. Patent Application Publication No. 2001/0046504 A1			401/402, Hearsay, Not Produced
PTX-210	EP 2 985 038			401/402, Hearsay, Not Produced
PTX-211	DE 19826517B4 (2006)			401/402, Hearsay, Not Produced
PTX-212	CN 102961343B (2012)			401/402, Hearsay, Not Produced
PTX-213	EP 2 745 833 A1			401/402, Hearsay, Not Produced
PTX-214	J. H. Beijnen et al., Chemical Stability of Two Sterile, Parenteral Formulations of Cyclophosphamide (Endoxan®) after Reconstitution and Dilution in Commonly used Infusion Fluids, PDA Journal of Pharmaceutical Science and Technology, Jul 1992, 46 (4) 111-116.			401/402, Hearsay, Not Produced
PTX-215	https://www.fresenius-kabi.com/us/news/fresenius-kabi-further-expands-oncology-portfoliowith-2024			401/402, Hearsay, Not Produced
PTX-216	https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/012141s089lbl.pdf			401/402, Hearsay, Not Produced
PTX-217	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/203856Orig1s000SumR.pdf			401/402, Hearsay, Not Produced
PTX-218	https://www.mims.com/hongkong/drug/info/endoxan?type=full			401/402, Hearsay, Not Produced
PTX-219	US Patent No. 5,418,223			401/402, Hearsay, Not Produced
PTX-220	US Patent No. 5,413,995			401/402, Hearsay, Not Produced
PTX-221	US Patent No. 5,268,368			401/402, Hearsay, Not Produced
PTX-222	US Patent No. 5,130,305			401/402, Hearsay, Not Produced
PTX-223	US Patent No. 4,659,699			401/402, Hearsay, Not Produced
PTX-224	US Patent No. 4,537,883			401/402, Hearsay, Not Produced
PTX-225	US Patent No. 5,066,647			401/402, Hearsay, Not Produced
PTX-226	PP&P 2024. CSTDs for Drug Preparation. S40. Pharmacy Purchasing & Products. April 2024			401/402, Hearsay, Not Produced

PTX-227	FDA Bioanalytical Method Validation: Guidance Industry, May 2018			401/402, Hearsay, Not Produced
PTX-228	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q8-q9-q10-questions-and-answers-appendix-qas-training-sessions-q8-q9-q10-points-consider			401/402, Hearsay, Not Produced
PTX-229	https://www.calculatorsoup.com/calculators/math/roundingnumbers.php			401/402, Hearsay, Not Produced
PTX-230	Sanpere Amat, E., Cyclophosphamide Sugar-coated Tablets			401/402, Hearsay, Not Produced
PTX-231	S. Nema et al., "Excipients and Their Role in Approved Injectable Current Usage and Future 12. Directions," PDA J Pharm Sci and Tech, Vol. 65 pp. 287-332 (2011)			401/402, Hearsay, Not Produced
PTX-232	WO 2017/207719			401/402, Hearsay, Not Produced
PTX-233	U.S. Patent Application Publication No. 20130172271 A1 (Fragale)			401/402, Hearsay, Not Produced
PTX-234	FDA GRASS list of solvents and excipients (GRASS: Generally Recognized As Safe Substances)			401/402, Hearsay, Not Produced
PTX-235	MPEP § 2141.01(a)			401/402, Hearsay, Not Produced
PTX-236	Dkt. 83, No. 1:22-cv-02868 No. 1:22-cv-02868 (N.D. Il. July 31, 2024)			401/402, Hearsay, Not Produced
PTX-237	Strickley, R., Solubilizing Excipients in Injectable Formulations, Pharmaceutical Research, Vol. 21, No. 2, February 2004			401/402, Hearsay, Not Produced
PTX-238	https://www.fda.gov/about-fda			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-239	https://www.fda.gov/drugs/types-applications/new-drug-application-nda			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-240	https://www.fda.gov/drugs/types-applications/abbreviated-new-drug-application-anda			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-241	https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/fda-list-authorized-generic-drugs			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-242	https://www.fda.gov/drugs/cder-conversations/generic-drug-approval-process			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-243	https://www.ingenus.com/about/			Excluded, 401/402, Hearsay, Not Produced, Foundation

PTX-244	http://leiutis.com/aboutus.php#intro_about			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-245	leiutis.com/whatwedo.php			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-246	leiutis.com/contactus.php			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-247	https://www.accordhealthcare.us/our-team/			Excluded, 401/402, Not Produced, Foundation
PTX-248	https://www.accordhealthcare.us			Excluded, 401/402, Not Produced, Foundation
PTX-249	https://www.intaspharma.com/about-us/overview/			Excluded, 401/402, Not Produced, Foundation
PTX-250	https://www.intaspharma.com/products/			Excluded, 401/402, Not Produced, Foundation
PTX-251	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/212501Orig1s000PharmR.pdf			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-252	https://www.cdc.gov/niosh/reproductivehealth/prevention/antineoplastic.html			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-253	https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2020/212501Orig1s000ltr.pdf			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-254	https://www.fda.gov/media/154797/download			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-255	Application to Market a New or Abbreviated New Drug or Biologic for Human Use	ACC-CYC0000019	ACC-CYC0000024	Excluded, 401/402
PTX-256	1.12.11 Basis for submission statement	ACC-CYC0000090	ACC-CYC0000091	Excluded, 401/402
PTX-257	https://www.uspto.gov/patents/basics/essentials			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-258	https://www.uspto.gov/patents/basics/manage#rights			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-259	Deposition of Dr. Samir Mehta, May 26, 2023			Excluded, 401/402, Hearsay, Not Produced, Foundation

PTX-260	Termination and Transfer of Rights Agreement effective June 6, 2024 between Ingenus and Leiutis Pharmaceuticals, Inc.	ING00133216	ING00133218	Excluded, 401/402, Hearsay, Foundation
PTX-261	Licence Agreement between Dr. Reddy's Labs and Ingenus Pharmaceuticals, Inc.	ING00133178	ING00133215	Excluded, 401/402, Hearsay, Foundation
PTX-262	https://www.wgrz.com/article/money/business/athenex-assets-sold-in-bankruptcy-auction-top-executivesdismissed/71-9cbc0f76-6419-4d03-bb6b-1c482de85ac6			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-263	https://www.globaldata.com/store/report/athenex-inc-company-profile/			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-264	https://www.post-journal.com/news/local-news/2023/06/coming-up-empty/			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-265	https://www.reuters.com/markets/deals/drugmaker-athenex-voluntarily-files-us-chapter-11-proceedings-2023-05-14/			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-266	Athenex, Inc. form 10-K for the fiscal year ended December 31, 2021			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-267	https://www.biospace.com/athenex-pharmaceutical-division-and-ingenus-pharmaceuticals-announce-availabilityof-liquid-ready-to-dilute-cyclophosphamide			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-268	https://www.accordhealthcare.us/company-profile/			Excluded, 401/402, Not Produced, Foundation
PTX-269	Ingenus sales data	ING00133327	ING00133327	Excluded, 401/402, Hearsay, Foundation
PTX-270	Ingenus sales data	ING00133328	ING00133328	Excluded, 401/402, Hearsay, Foundation
PTX-271	1.14.1.2 ANNOTATED DRAFT LABELING TEXT	ACC-CYC0000032	ACC-CYC0000048	Excluded, 401/402
PTX-272	https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/excipient			Excluded, 401/402, Hearsay, Not Produced, Foundation
PTX-273	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/212501Orig1s000ClinPharmR.pdf			401/402, Hearsay, Not Produced, Foundation
PTX-274	Approval Letter for NDA 212501 dated 7/30/2020 (with enclosures)	ING00012106	ING00012131	
PTX-275	Approval Letter for NDA 212501 dated 7/30/2020	ING00103474	ING00103478	
PTX-276	curriculum vitae for Alpaslan Yaman			
PTX-277	curriculum vitae for William Zamboni			

EXHIBIT 8

UNREDACTED PUBLIC VERSION

Ingenus Pharmaceuticals, LLC and Leiutis Pharmaceuticals LLP v. Accord Healthcare, Inc.
23-cv-00377-JLH

Trial Dates: March 24-27, 2025

ACCORD'S EXHIBIT LIST

DTX NO.	Description	Bates Beg No.	Bates End No.	Dep Ex. No.	Expert Exhibit #	Objections
1	United States Patent No. 10,993,952				McConville Ex. 1	
2	File History for United States Patent No. 10,993,952				McConville Ex. 2	
3	United States Patent No. 4,879,286 (Alam)				McConville Ex. 3	
4	United States Patent Application Publication No. 2015/0320775 (Palepu)			Zamboni 2; Yaman 9	McConville Ex. 4	
5	United States Provisional Patent Application No. 61/991,247 (Palepu				McConville Ex. 5	
6	WO 2016/005962 (Shaik)				McConville Ex. 6	
7	3454/CHE/2014 (Shaik 3454)				McConville Ex. 7	AU
8	5215/CHE/2014 (Shaik 5215)				McConville Ex. 8	AU
9	United States Patent No. 4,952,575 (Sauerbier)				McConville Ex. 9	
10	WO 02/02125 (Tait)			Yaman 11	McConville Ex. 10	
11	Brazeau, G & Fung, HL, *Mechanisms of Creatine Kinase Release from Isolated Rat Skeletal Muscles Damages by Propylene Glycol and Ethanol* , 79(5) J Pharmaceutical Sciences 393 (May 1990)				McConville Ex. 11	AU, R
12	FDA Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products				McConville Ex. 14	
13	NDA 210735 Approval Letter				McConville Ex. 15	AU, R
14	Auromedics Label				McConville Ex. 16	AU, R

Ingenus Pharmaceuticals, LLC. and Leiutis Pharmaceuticals LLP v. Accord Healthcare, Inc.
23-cv-00377-JLH

Trial Dates: March 24-27, 2025

ACCORD'S EXHIBIT LIST

DTX NO.	Description	Bates Beg No.	Bates End No.	Dep Ex. No.	Expert Exhibit #	Objections
15	B. Nagaraju Declaration 10-1-19	ING00000231	ING00000238	Nagaraju Ex. 2		
16	B. Nagaraju Declaration 4-8-20	ING00000146	ING00000150	Nagaraju Ex. 3		
17	Chandrashekar Declaration 10-1-19	ING00000239	ING00000246	Chandrashekar Ex. 3		
18	Chandrashekar Declaration 4-8-20	ING00000151	ING00000155	Chandrashekar Ex. 4		
19	Chandrashekar Declaration 1-14-21	ING00000085	ING00000089	Chandrashekar Ex. 5		
20	Accord ANDA Section 3.2.P.1	ACC-CYC0036605	ACC-CYC0036605		Yaman Ex. G	X
21	Accord ANDA Section 1.12.15	ACC-CYC00000217	ACC-CYC00000217	Singh Ex. 17		
22	Jason McConville CV				McConville Ex. A	A
23	Ingenus label	ING000041446			Zamboni ¶ 78	
24	Ingenus Package Insert			Zamboni 3		AU, R, X, Z
25	BioSpace webpage, December 2, 2020			Zamboni 4		AU, R, X, Z
26	Announcement by Eugia re: AuroMedics Pharma			Zamboni 5		AU, R, X, Z
27	Center for Drug Evalutaion and Research Approval, August 25, 2021			Zamboni 6		AU, R, X, Z
28	Baxter package insert, revised April 2012			Zamboni 7		AU, R, X, Z
29	Cyclophosphamide Injection 200 mg/mL	ACC-CYC0000305	ACC-CYC0000388	Yaman 4	Yaman Ex. C	
30	Cyclophosphamide Injection 200 mg/mL - Description and Composition of the Drug Product	ACC-CYC0036605	ACC-CYC0036606	Yaman 5	Yaman Ex. G	

Trial Dates: March 24-27, 2025

ACCORD'S EXHIBIT LIST

DTX NO.	Description	Bates Beg No.	Bates End No.	Dep Ex. No.	Expert Exhibit #	Objections
31	Responsive Expert Report of Jason McConville, Ph.D. Regarding Non-Infringement of U.S. Patent No. 10,993,952, December 6, 2024			Yaman 6		AU, H
32	U.S. Pharmacopeia National Formulary Volume 2 (2011)			Yaman 10		AU, R, X, Z
33	Kibbe, Arthur, Handbook of Pharmaceutical Excipients, Third Edition			Yaman 12		AU, R, X, Z

EXHIBIT 9

UNREDACTED PUBLIC VERSION

EXHIBIT 9

PLAINTIFFS' WITNESS LIST

Plaintiffs Identify the following witness whom it may call live or by deposition at trial. This list is not a commitment that plaintiff will call any particular witness at trial, or representation at any of the witnesses listed are available or will appear for trial. With respect to defendant's witnesses, plaintiffs reserve the right to introduce testimony through deposition or live examination, as appropriate. Plaintiffs also reserve the right to call any witnesses called by defendants, and to revise this list in light of further rulings by the court or any other changed circumstances. Plaintiffs further reserve the right to call one or more additional witnesses whose testimony is necessary to establish authenticity or admissibility of any trial exhibit if the admissibility of the exhibit is challenged by defendant.

I. Expert Witnesses

Below are the expert witnesses plaintiffs propose to call as live witnesses at trial.

1. Alpaslan Yaman, Ph.D.

Dr. Yaman is an expert in pharmaceutical sciences, especially pharmaceutical product development: pre-formulations, formulations, process development and scale-up (for sterile and non-sterile liquids and semisolid products such as complex emulsions and suspensions including controlled release, e.g. liposomes and microspheres); tech transfer, commercialization, process validation, and PAI readiness and support; equipment qualification, process automation, and Sterile Manufacturing; and cGMP and Regulatory Applications (specifically pertaining to CMC sections of IND, NDA, BLAs, and PMA). He has received numerous awards from internal and external organizations, including those from Johnson & Johnson and the American Association of

Pharmaceutical Scientists (AAPS), as well as the President's Award by Schering-Plough Research Institute (SPRI), for process improvements and scale up of a dual-chambered lyophilized protein.

He has scaled up and validated more than 40 products ranging from sterile powders to lyophilized reconstituted products. He has authored numerous publications and has been selected as a Subject Matter Expert (SME) by International Soc. Pharm Eng. In the areas of Pharmaceutical Product Development: pre- formulations, formulations, process development and scale-up. Dr. Yaman will testify regarsing the infringement and validity of the '952 Patent.

2. William Zamboni, PharmD, Ph.D.

Dr. Zamboni is an expert in drug development, translational pharmacology (preclinical and clinical), pharmacokinetic, pharmacodynamic, and biomarker studies of small molecule and complex (e.g., nanoparticles, conjugates, and biologics) agents. He has worked as a pharmacist and/or prepared IV medications, including chemotherapy, for patients and as part of animal studies. He has significant experience preparing reconstituted powder forms of injectable drugs, as well as preparing IV infusions from RTU formulations while working at the National Institutes of Health, St. Jude Children's Hospital, University of Maryland, University of Pittsburgh, Pittsburgh Children's Hospital, and the University of North Carolina.

He is a Tenured Professor in the Division of Pharmacotherapy and Experimental Therapeutics in the University of North Carolina (UNC) at Chapel Hill Eshelman School of Pharmacy (ESOP) and a Research Associate Professor in the Department of Pharmacology in the School of Medicine (SOM) at UNC. He is also a Member of the Molecular Therapeutics Program in the UNC Lineberger Comprehensive Cancer Center (LCCC) and the Carolina Institute for Nanomedicine (CINM). He has over 190 peer-reviewed publications that are published or in press

in well recognized journals, and over 170 abstracts presented or published at scholarly and professional conferences. He has served on various editorial Boards and is he named inventor on a U.S. Patent. Dr. Zamboni will testify about the differences between powdered formulations for reconstitution and RTU/RTA formulations and the advantages and disadvantages of each.

II. Fact Witnesses

1. Kocherlakota Chandrashekar
2. Banda Nagaraju
3. Kuldeep Karnik
4. Ajeet Singh
5. Sabita Nair

Exhibit 10

UNREDACTED PUBLIC VERSION

Alpaslan Yaman, Ph.D.
ayaman@biopharmadvice.com
(973) 896 8047

CAREER SUMMARY

Ph.D. in Pharmaceutical Sciences and a J&J Certified Process Excellence (6-Sigma) Black Belt. Over 32 years of experience in the biotech, pharmaceutical and medical device industry in sterile and non-sterile formulation development, process development (including automation) and scale-up, validation, technology transfer and technical services, also experienced with Parenteral facility design and validation. Have scaled up and validated more than 40 products ranging from sterile powders to lyophilized reconstituted products. Have working experience with gamma irradiation of macromolecules, microwave sterilization, and with blow/fill/seal technology. Have working experience with both traditional and biotech (peptides, proteins and nucleotide) drugs and drug delivery systems such as emulsions, suspensions, nanoparticles, liposomes, microspheres and drug/device combination products. Have served as a task force member in the validation of 2 facilities and am experienced with facilities in Sweden, Switzerland, France, Germany, Austria, Puerto Rico, Ireland and Singapore. In addition, am experienced with preapproval inspections both here in the US and in Europe involving the FDA and the EMA. Have extensive experience with third party CDMO and CMO manufacturers and service providers both in the arena of technical support and quality/compliance. Have experience with the performance of quality compliance audits (QSR, GXP: GDP, GMP and GLP).

EDUCATION

Ph.D. in Pharmaceutical Science (Major in Industrial Pharmaceutics with minor in Physical Chemistry) from the University of Missouri, Kansas City, Missouri in 1992. BS in Pharmacy in 1987 and BA in Chemistry and Biology in 1984 from Drake University, Des Moines, IA.

EXPERIENCE

Biotech, Pharma & Device Consulting, LLC
www.biopharmadvice.com
(1/09 – Present)

Principal Consultant.
Am providing technical review and input as an independent contract technical resource for the Biotech, Pharmaceutical and Medical Device (with specific emphasis on drug/device combination products) industries.

In addition to providing technical consulting with regards to development and commercialization of complex product and processes, I provide compliance support which includes development of quality systems and remediation that is specific to the size and need of the company. Throughout my years and experience with product development, I have never received a FD 483 or negative citation from the FDA. Also, available experience with site inspections in North America, Europe and South-East Asia.

Finally, have extensive experience as an Expert Witness in Patent Litigation, both IPRs and Litigation in Federal Court and in the negotiations of contracts with suppliers and third-party contract manufacturing service providers.

Edge Therapeutics, Inc.
www.edgetherapeutics.com
(2/2014 – 5/2018)

Vice President, Operations and Manufacturing
Part of Senior Leadership reporting to the Chief Executive Officer, responsible for the commercial manufacture and supply of both active pharmaceutical ingredients and the finished pharmaceutical product worldwide. Included in my responsibilities, negotiations of commercial supply agreements with vendors and contract manufacturing organizations. Also, responsible for the Chemistry, Manufacturing and Controls of all products in the pipeline from early concept through commercialization supporting product development with oversight through IND and NDA filings.

QbD Auditing, Inc.
Website: www.qbdauditing.com
(7/09 – 7/13)

Cofounder – Principal Consultant
This is a newly formed company which is actively working with regulated industries to provide technical assessments and c'GXP audits of all aspects of their operation with recommendations for mitigation of risk.

Johnson & Johnson
Cordis Corp.
(4/05 – 12/08)

Sr. Research Fellow, Product Support/Technical Services (4/2007 – 12/2008).
Responsibilities included providing base business support as a Subject Matter Expert (SME) for drug/device combination products, by leading or supporting directly the product improvement of commercial products, as well as process optimizations for the operational sites in the manufacturing of a wide variety of medical device products. Prepared project plans and involved with design review, PMA submissions and PAI readiness.

Executive Director, Process Engineering, Worldwide Technical Operations (4/2005 – 4/2007).
Responsible for three process engineering groups: Drug / Device Combination Products, Cardiology and Endovascular/Neurovascular Device. Responsibilities included leading and directing technology transfer through PQ and PPQ of device and drug/device products, as well as process optimizations and base business support for the operational sites in the manufacturing of a wide variety of medical device products. Prepared project strategy plans and involved with design review, PMA submissions and PAI readiness. Served as the Technical Operations representative member on the project team to ensure that the final process was commercially feasible and efficient.

Worked towards the development of a training module to provide a basic pharmaceutical science understanding within the organization to facilitate and drive for future success within the development of drug/device combination products.

Schering-Plough
Kenilworth, NJ
(7/30/01 – 3/31/2005)

Director, Pharmaceutical Technology Transfer, Global Technical Services (7/01 – 3/31/2005).
Responsibilities included leading and directing technology transfer through the scale-up and validation of sterile and non-sterile liquid and semisolid pharmaceutical products. Preparing technology transfer, strategy plans, and GAP analysis for project transfers between development and operations or from one operating Site to another. Served as the Technical Operations representative member on the project team, the CMC sub-team, and the technology transfer team to insure that the final process was commercially feasible and efficient.

Purdue Pharma, L.P.
Ardsley, NY
(8/99 – 7/01)

Assistant Director, Parenteral Technology Transfer, Parenteral Formulations (8/99 – 7/01).
Responsibilities included leading and directing the technology transfer group through the scale-up and validation of parenteral products. Also involved with equipment acquisitions, the writing and reviewing of equipment specifications and related SOPs. Prepared and executed protocols for process and equipment

validations (e.g. IQOQPQ). Involved in the optimization of complex processes for the manufacture of injectable controlled release formulations. Involved in the development of the CMC section for NDA and BLA submission and with preapproval inspections.

Novartis Pharmaceuticals, Inc.
E. Hanover, NJ
(5/97- 8/99)

Research Fellow II, Pharmaceutical Development (1/99 – 8/99). Responsibilities included leading and directing a group through the early development, scale-up and validation of liquid pharmaceutical commercial processes (oral liquids and sterile products). Worked with multidisciplinary groups to assess the feasibility of new chemical entities. Involved with the identification of new technologies, equipment acquisitions, and the writing and reviewing of equipment specifications and related SOPs. Prepared and executed protocols for process and equipment validations (e.g. IQOQPQ). Involved in the development of the CMC section for NDA and BLA submission and with preapproval inspections.

Assistant Director, Process Research and Development, Head, Liquids/Technical Life Cycle Management (5/97 - 1/99). Responsibilities included leading and directing the liquids group through the scale-up and validation of liquid pharmaceutical commercial processes (oral liquids and sterile products). Also involved with equipment acquisitions, the writing and reviewing of equipment specifications and related SOPs. Prepared and executed protocols for process and equipment validations (e.g. IQOQPQ). Involved in the development of the CMC section for NDA and BLA submission and with preapproval inspections.

Hoffmann-LaRoche
Nutley, NJ
(4/96-4/97)

Pharmaceutical Process Investigator (Roche manager level), Pharmaceutical Process and Technical Development in the Process and Package Development Department (4/96-4/97). Responsibilities included the scale-up and validation of sterile pharmaceutical commercial processes. Also involved with equipment acquisitions, the writing and reviewing of equipment specifications and related SOPs. Prepared and executed protocols for process and equipment validations (e.g. IQOQPQ). Involved in the development of the CMC section for NDA and BLA submission and with preapproval inspections.

Also involved as the chairman of the Co-Development Team and liaison to the International Project Team from the Pharmaceutical Operations area. This involved the leading of multidisciplinary teams consisting of personnel from all departments associated with bringing products from Phase II through validation and on to launch.

Johnson & Johnson
The R.W. Johnson Pharmaceutical Research Institute
Raritan, NJ
(12/92-4/96)

Senior Scientist, Parenterals, Pharmaceutical Process Development and Technical Service in the Department of Pharmaceutical Development and Technical Service (1/95-4/96) Responsibilities included the scale-up and validation of sterile pharmaceutical commercial processes. Also involved with the set-up, design, and validation of parenteral manufacturing facilities in the US and Europe. Involved in the development of the CMC section for NDA, BLA, and dossier submissions and with preapproval inspections.

Scientist, Parenterals, Pharmaceutical Process Development and Technical Service in the Department of Pharmaceutical Development and Technical Service (12/92-1/95) Responsibilities included the scale-up

and validation of sterile pharmaceutical commercial processes. Also involved with the set-up, design, and validation of parenteral manufacturing facilities in the US and Europe. Involved in the development of the CMC section for NDA, BLA, and dossier submissions and with preapproval inspections.

Fujisawa, USA
Melrose Park, IL
(3/92-11/92)

Senior Scientist, Product Transfer of the Corporate Quality Assurance Department (3/92-11/92). Responsibilities included the scale-up and validation of sterile pharmaceutical commercial processes. Also, wrote and executed IQOQPQ equipment protocols for validation of a facility under a Consent Decree. The inspection of facilities for cGMP compliance with participation in the task force for the reconciliation of technical service issues.

OTHER EXPERIENCE
Staff Pharmacist
Kansas City, MO
(9/87-2/92)

Worked as a staff Pharmacist for various hospital and retail settings. Experience proved valuable in understanding how products are used in the clinical and retail settings and provided insight for later commercial product development.

Marion Laboratories
Kansas City, MO
(5/89-8/89)

Graduate Research Intern, responsible for the determination of the collapse temperature for a collagen slurry (artificial skin product) and lyophilization optimization in the pilot and production facility.

Sandoz Research Institute
E. Hanover, NJ
(5/86-10/86 & 5/87-8/87)

Research Intern, responsible for experiments in the development of transdermal and iontophoretic patches for a peptide product. Developed of a computer integrated automated HPLC/diffusion set-up and refined as necessary the required analytical methods.

PUBLICATIONS & PRESENTATIONS
Alpaslan Yaman (2012), "Methods of Sterilization for Controlled Release Injectable and Implantable Preparations", Controlled Release Science and Technology: Long acting injections and implants Edited J. Wright and D. Burgess, New York, Springer.

Alpaslan Yaman, "Leveraging Documents in Medical Device Development," Medical Device & Diagnostic Industry (MDDI): Sept. 2009, p.32.

Alpaslan Yaman, "Alternative Methods of Terminal Sterilization for Biologically Active Macromolecules," Current Opinion in Drug Discover & Development (2001) 4:760-763.

Lally Samuel, Monica A. Kwarcinski and Alpaslan Yaman**, "**Compatibility and Stability of Levobupivacaine Infusion Bags With Fentanyl or Clonidine," American Journal of Health-System Pharmacy. 58(20); 1962-1982, October 15, 2001.

Alpaslan Yaman (1995) “Engineering Considerations in Sterile Powder Processes”, Sterile Pharmaceutical Products: Process Engineering Applications, Edited Kenneth E. Avis, INTERPHARM Press.

Alpaslan Yaman (1992) “Process Development for Air-Free Injectables” Dissertation.

Alpaslan Yaman, “Science-Based Product Development”, Invited Speaker, New Jersey Pharmaceutical Association for Science and Technology (NJPhAST), Washington Township, NJ (December 2007).

Alpaslan Yaman, "Alternative Methods of Terminal Sterilization", Invited Speaker, International Society of Pharmaceutical Engineers (ISPE) Winter Conference, Tampa, FL (February 2006).

Alpaslan Yaman, “Science-Based Product Development”, Invited Speaker, Food and Drug Administration (FDA), Rockville, MD (September 2004).

Alpaslan Yaman, “Alternative Methods of Terminal Sterilization”, Invited Speaker, PDA SciTech Summit, Orlando, FL (March 9, 2004).

Alpaslan Yaman, “Science-Based Process Validation”, Invited Speaker, 39th Annual Pharmaceutical Technologies Conference at Arden House (AAPS: Jan. 2004).

Alpaslan Yaman, “Alternative Methods of Terminal Sterilization”, symposium AAPS Annual Meeting, Toronto, ONT (2002).

Alpaslan Yaman, “Full Scale-up – Liquids”, 35th Annual Pharmaceutical Technologies Conference at Arden House Conference (AAPS: Jan. 2000).

Alpaslan Yaman, Robert Butler, and Hirayuki Takashima, “Sparging Optimization for Oxidation Labile Drugs in Parenteral Solutions” AAPS Ninth Annual Meeting (1994).

Alpaslan Yaman and Lester Chafetz, “Process Development for Air-Free Injectables” AAPS Sixth Annual Meeting (1991)

B.A. Clark and A. Yaman, “Calorimetric and Conductimetric Determination of Collapse Temperature of Collagen Co-Precipitates and Application in Lyophilization Development” AAPS Fourth Annual Meeting (1989)

HONORS
Selected as Subject Matter Expert (SME) by International Soc. Pharm Eng. (ISPE: 2007)
Recognized areas of expertise:

1. Pharmaceutical Product Development: pre- formulations, formulations, process development and scale-up (for sterile and non-sterile liquids and semisolid products including controlled release)
2. Tech transfer, Commercialization, Process Validation and PAI Readiness and Support
3. Equipment Qualification, Process Automation and Sterile Manufacturing
4. cGMP, Regulatory Applications (specifically pertaining to CMC sections of IND, NDA, BLAs and PMA)

Sr. Research Fellow – Johnson & Johnson Corporate Office of Science and Technology (2007)
Team Excellence Award – Cordis Corp (2005)
President’s Award Schering-Plough Research Institute (2003)
Leadership Awards – AAPS (2000 & 2003)
Member of RHO CHI
Marion Laboratories Fellowship in Pharmaceutical Technology (1989-1990)

Chancellor's Award, University of Missouri-Kansas City (1988-1991)
Marion Laboratories Summer Graduate Research Internship (1989)
NPC Research Intensive Internship - Sandoz Research Institute (1986)

ORGANIZATIONS
American Chemical Society (ACS)
American Association of Pharmaceutical Scientist (AAPS)
Parenteral Drug Association (PDA)
International Society of Pharmaceutical Engineers (ISPE)
New Jersey Pharmaceutical Association of Science and Technology (NJPhAST)

TRAINING
Process Excellence (DMAI^{2}C Certified Blackbelt: J&J)
Lean Champion Training (J&J)
Project Management

OTHER ACTIVITIES
Invited to participate in the ISPE Examination Development Committee for the development of certification examination questions for the CPIP (Certified Pharmaceutical Industry Professional) program.
Referee for manuscripts submitted for publication in Pharmaceutical Research (AAPS) (2003 – 2005)
Vice Chair, Chair-Elect, Chair and Past Chair, Pharmaceutical Technology (PT) Section of American Association of Pharmaceutical Scientist (AAPS) (2001-2005).
Arden House Conference 2000, "Technical Transfer of Pharmaceutical Products from the Laboratory to Commercial Production", Planning Committee Chair (1999-2000)
Chairman of the Paperscreening Committee, Pharmaceutical Technology (PT) Section (AAPS) (1998)
President, Pharmaceutical Sciences Graduate Student Association (PSGSA) (1989-1991).
Voting Member, Graduate Programs & Admission Committee, School of Pharmacy (1989-1991).
Vice President, Pharmaceutical Sciences Graduate Student Association (PSGSA) (1987-1989).

CURRICULUM VITAE

William C. Zamboni, Pharm.D., Ph.D.

PERSONAL INFORMATION

Office Address: Division of Pharmacotherapy and
Experimental Therapeutics
UNC Eshelman School of Pharmacy
University of North Carolina at Chapel Hill
1013 Genetics Medicine Building
120 Mason Farm Road, CB 7361
Chapel Hill, NC 27599-760
Office Phone: 919.843.6665
Fax: 919.966.5863
Lab Phone: 919.966.9866
Cell Phone: 412.951.0480
Email: zamboni@unc.edu

EDUCATION AND TRAINING

Doctor of Philosophy 2001 - 2005
Clinical Pharmaceutical Scientist Program
Dept. of Pharmaceutical Sciences, University of Pittsburgh, School of Pharmacy, Pittsburgh, PA. Dissertation was titled "Preclinical and Clinical Pharmacologic Studies of 9-nitrocamptothecin and its 9-aminocamptothecin metabolite".

Research Fellowship 1995 - 1997
Department of Pharmaceutical Sciences
St. Jude Children's Research Hospital, Memphis, TN.

Oncology Pharmacy Residency 1994 - 1995
Warren G. Magnuson Clinical Center, National Institutes of Health, Bethesda, MD.

Doctor of Pharmacy 1992 - 1994
University of Pittsburgh School of Pharmacy, Pittsburgh, PA.

Bachelor of Science in Pharmacy 1988 - 1992
University of Pittsburgh School of Pharmacy, Pittsburgh, PA.

PROFESSIONAL EXPERIENCE

ACADEMIC

Current Academic Positions at UNC:

Professor 2022 - Present

Division of Pharmacotherapy and Experimental Therapeutics
UNC Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC.
(Associate Professor from 2008 - 2022)

Research Associate Professor 2014 - Present
Department of Pharmacology
UNC School of Medicine, University of North Carolina, Chapel Hill, NC.

Current Research Positions at UNC:

Director, UNC Advanced Translational Pharmacology 2020 - Present
and Analytical Chemistry (A-TPAC) Lab and Recharge Center.
UNC Eshelman School of Pharmacy and UNC Lineberger
Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC.

Co-Faculty Director, Nanomedicines Characterizations Core 2014 - Present
UNC Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC.

Member, Center for Nanotechnology in Drug Delivery 2014 - Present
UNC Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC.

Member, Carolina Institute of Nanomedicine 2012 - Present
University of North Carolina, Chapel Hill, NC.

Director, Analytical Chemistry and Pharmacology Core Lab 2010 - Present
UNC Lineberger Comprehensive Center.

Director, Oncology Research and Drug Development Fellowship Program 2009 - Present
UNC Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC.

Director, Translational Oncology and Nanoparticle Drug Development 2008 - Present
Initiative ($TOND_2I$) Lab, UNC Eshelman School of Pharmacy and
UNC Lineberger Comprehensive Cancer Center
University of North Carolina, Chapel Hill, NC.

Member, Molecular Therapeutics Program 2008 - Present
UNC Lineberger Comprehensive Cancer Center
University of North Carolina, Chapel Hill, NC.

Member, Center for Pharmacogenomics and Individualized Therapy 2008 - Present
University of North Carolina, Chapel Hill, NC.

Prior Positions at UNC:

Associate Professor 2008 - 2022
Division of Pharmacotherapy and Experimental Therapeutics
UNC Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC.

Co-Director, Mouse Phase I Unit 2009 - 2015
UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC.

Co-Director, NC Biomedical Innovation Network 2009 - 2012
Research Triangle Park, NC.

Member, Carolina Center of Cancer Nanotechnology Excellence 2008 - 2020
University of North Carolina, Chapel Hill, NC.

Director, UNC GLP Bioanalytical Facility 2008 - 2014
UNC Eshelman School of Pharmacy and UNC Lineberger
Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC.

Member, Center for Experimental Therapeutics 2008 - 2010
University of North Carolina, Chapel Hill, NC.

<u>Prior Positions Not at UNC</u>:

Assistant Professor 2007 - 2008
Department of Obstetrics Gynecology, and Reproductive Sciences
School of Medicine, University of Pittsburgh, Pittsburgh, PA.

Adjunct Clinical Instructor 2001 - 2013
Department of Pharmacy Practice
School of Pharmacy, Duquesne University, Pittsburgh, PA.

Assistant Member, Molecular Therapeutics Drug Discovery Program 1998 - 2008
University of Pittsburgh Cancer Institute
University of Pittsburgh Health System, Pittsburgh, PA.

Assistant Professor, Department of Pharmaceutical Sciences 1998 - 2008
School of Pharmacy, University of Pittsburgh, Pittsburgh, PA.

Assistant Professor, Division of Hematology-Oncology 1998 - 2008
Department of Medicine, School of Medicine
University of Pittsburgh, Pittsburgh, PA.

Assistant Professor, Department of Developmental Therapeutics 1997 - 1998
Greenebaum Cancer Center, University of Maryland, Baltimore, MD.

Clinical Assistant Professor, Department of Pharmacy Practice and Science 1997 - 1998
School of Pharmacy, University of Maryland, Baltimore, MD.

<u>NON-ACADEMIC</u>:

<u>Current Positions</u>:

NuVeta Radiotherapy 2023 - Present
Member, Scientific Advisory Board
Company specializes using novel radiation technology to increase the delivery of drugs to tissues.
Durham, NC

HealthSpan Research 2023 - Present
Chief Scientific Officer
Company specializes in developing therapeutic agents to extend a person's health span.
Boston, MA

U.S. FDA
Member, Pharmaceutical Science and Clinical Pharmacology Advisory Committee 2022 - Present
of the US Food and Drug Administration, Silver Spring, MD

St. Jude Children's Research Hospital
Member, St. Jude Comprehensive Cancer Center Pharmacokinetic Shared Resource External Advisory Board, Memphis, TN — 2022 - Present

Akagera Medicines — 2020 - Present
Member, Scientific Advisory Board
Company specializes in targeting tuberculosis and other infectious diseases with liposomal therapeutics.
Boston, MA

Glolytics, LLC — 2016 - Present
Chief Scientific Officer and Founder
Company specializes in the evaluation of the bi-directional interaction between the immune system and drugs, nanoparticles, antibodies, ADCs and biological agents
Chapel Hill, NC

ChemoGLO, LLC — 2012 - Present
Chief Scientific Officer and Co-Founder
Company specializes in the detection and removal of hazardous drugs in hospitals, laboratories and manufacturing facilities
Chapel Hill, NC

MediGLO, LLC — 2006 - Present
Chief Executive Officer and Founder
Company focuses on medical, pharmaceutical and drug development consulting
Chapel Hill, NC

Prior Positions:

Member, Petersen Institute of NanoScience and Engineering — 2006 - 2008
University of Pittsburgh, Pittsburgh, PA.

Staff Pharmacist — 1999 - 2006
Children's Hospital of Pittsburgh, Pittsburgh, PA.

Staff Pharmacist — 1998 - 1998
Pharmacy Department., NIH, Bethesda, MD.

Staff Pharmacist — 1993 - 1994
Veteran's Affairs Medical Center, Pittsburgh, PA.

Staff Pharmacist — 1992 - 1994
PRS Consultants, Latrobe, PA.

Staff Pharmacist — 1992 - 1994
Children's Hospital of Pittsburgh, Pittsburgh, PA.

Staff Pharmacist — 1992 - 1992
Rinehart's Pharmacy, Nanty Glo, PA.

LICENSURE AND CERTIFICATION

Pharmacy License (Pennsylvania #RP039278L) — 1992 - Present

HONORS AND AWARDS

Triangle Business Journal BDO Life Sciences Award – Outstanding Biotech Company (ChemoGLO, LLC) from a Research University	2015
American College of Clinical Oncology Aventis Oncology Fellowship entitled "Evaluation of the Tumor Disposition of Cisplatin using Microdialysis in Patients with Melanoma."	2001
Phi Delta Chi Distinguished Alumni Award American College of Clinical Pharmacy Rhone-Poulenc Rorer 1999 Oncology Research Award entitled "Disposition of Liposomal-Cisplatin (SPI-77) and Cisplatin in Solid Tumors"	1999
American College of Clinical Pharmacy Rhone-Poulenc Rorer 1996-97 Oncology Fellowship Research Project entitled: "Cerebrospinal Fluid (CSF) Disposition of Topoisomerase I Inhibitors in the Nonhuman Primate Model"	1997
American Society of Clinical Oncology 1997 Merit Award for the presentation entitled: "Pharmacokinetically Guided Dose Adjustment Reduces Variability in Topotecan (TPT) Systemic Exposure in Children with Solid Tumors".	1997
American College of Clinical Oncology Phone-Poulenc Rorer Oncology Fellowship entitled "Cerebrospinal Fluid (CSF) Disposition of Topoisomerase I Inhibitors in a Nonhuman Primate Model"	1996
American Society of Clinical Oncology 1996 Merit Award for the presentation entitled: "Pharmacokinetics (PK) of Topotecan (TPT) in Pediatric Patients with Normal and Altered Renal Function".	1996
Magna Cum Laude, Doctor of Pharmacy Program, University of Pittsburgh	1994
University of Pittsburgh Alumni Association Graduate Scholarship	1993
University of Pittsburgh Honors Convocation Honoree	1992
Eli Lilly Achievement Award for Ethics, Scholarship and Leadership	1992
University of Pittsburgh University Scholar	1992
Magna Cum Laude, University of Pittsburgh School of Pharmacy	1992
University of Pittsburgh Student Leadership Honor Society	1992
Emma W. Locke Memorial Award Nominee	1992
Omicron Delta Kappa National Leadership Honor Society	1992
Rho Chi Pharmacy Honor Society	1991
University of Pittsburgh Honors Convocation Honoree	1991

BIBLIOGRAPHY

PATENTS

1. Method and System for Hazardous Drug Surface Cleaning. By William Zamboni, Tom O'Neill, and Stephen Eckel. Patent Number US 11,274,271. March 15, 2022.

PUBLICATIONS

Chapters or Review Articles

Published or in Press

1. **Zamboni WC,** Orbach R, Burckart GJ, Stewart CF. Effect of Obesity on the Pharmacokinetics and Pharmacodynamics of Anticancer Agents. Journal of Clinical Pharmacology. 2023;63(S2) S85-S102. [Part of Journal of Clinical Pharmacology supplement entitled Bridging Drug Efficacy and Safety to the Obese].

2. McColl ER, Croyle MA, **Zamboni WC**, Honer WG, Heise M, Piquette-Miller M, Goralski KB. COVID-19 Vaccines and the Virus: Impact on Drug Metabolism and Pharmacokinetics. Drug Metab Dispos. 2023 Jan;51(1):130-141. doi: 10.1124/dmd.122.000934. Epub 2022 Oct 23. PMID: 36273826.

3. Lucas AT, Moody A*, Schorzman AN, **Zamboni WC**. Importance and Considerations of Antibody Engineering in Antibody-Drug Conjugates Development from a Clinical Pharmacologist's Perspective. Antibodies (Basel). 2021 Jul 26;10(3):30. doi: 10.3390/antib10030030. PMID: 34449544; PMCID: PMC8395454.

4. Moody AS*, Dayton P, Lucas AT, **Zamboni WC**. Imaging methods to evaluate tumor microenvironment factors affecting drug delivery and predict antitumor response. Overcome Cancer Drug Resistance by Nano-carrier Drug Delivery System. Editor: Vladimir P. Torchilin. Cancer Drug Resist. 2021;4:382-413. doi: 10.20517/cdr.2020.94. Epub 2021 Jun 19.

5. Piscitelli JA*, Ban Jisun*, Lucas AT, **Zamboni WC**. Complex factors and challenges that affect the pharmacology, safety and efficacy of Nanocarrier Drug Delivery Systems. Overcome Cancer Drug Resistance by Nano-carrier Drug Delivery System. Pharmaceutics. 2021; 13(1): 114.

6. Lucas AT*, Robinson R, Schorzman AN, Piscitelli J*, Razo J*, **Zamboni WC**. Pharmacologic considerations in the disposition of antibodies and antibody-drug conjugates in preclinical models and in patients. Antibodies. 2019; 8(1): 3. doi: 10.3390/antib8010003. PMID: 31544809.

7. **Zamboni WC**, Szebeni J, Kozlov V, Lucas AT, Piscitelli JA*, Dobrovolskaia MA. Animal Models for Analysis of Immunological Responses to Nanomaterials: Challenges and Considerations. Adv Drug Deliv Rev. 2018 Nov - Dec;136-137:82-96. PMID: 30273617.

8. Lucas AT, Price LSL*, Schorzman AN, Storrie M*, Piscitelli JA*, Juan Razo, **Zamboni WC**. “Factors affecting the pharmacology of antibody-drug conjugates”. Antibodies. 2018; 7(1): 10. doi: 10.3390/antib7010010. PMID: 31544862

9. Schorzman AN, Lucas AT*, Kagel JK*, **Zamboni WC**. Methods and Study Designs for Characterizing the Pharmacokinetics and Pharmacodynamics of Carrier-Mediated Agents. Methods Mol Biol. 2018;1831:201-228. PMID: 30051434.

10. Lucas AT*, Price LS*, Schorzman AN, **Zamboni WC**. Complex effects of tumor microenvironment on the tumor disposition of carrier-mediated agents. Invited review, Nanomedicine. 2017:12(16):2021-2042. PMID: 28745129.

11. Tyson R*, Osae L*, Madden AJ*, Lucas AT*, **Zamboni WC**. Preclinical and Clinical Pharmacology Studies of Nanoparticles: The Translational Challenge. Nanopharmacy, 1st Edition, Wileys. 2017.

12. Tamarkin L, Yuan Z, Maggi EC, Adem A, Schorzman AN, **Zamboni WC**, Oarr D, Libutti SK. Cancer Nanomedicines: Opportunities and Challenges. Biotech, Biomaterials and Biomedical - TechConnect Briefs. 2017; 3:126-129.

13. Proctor AE, **Zamboni WC**. Ovarian cancer. In: Schwinghammer TL et al, eds. Pharmacotherapy Casebook: A Patient-Focused Approach. 10th ed. New York: McGraw-Hill, 2017.

14. Lucas AT*, Madden AJ*, **Zamboni WC**. Challenges in preclinical to clinical translation for anticancer carrier-mediated agents. Invited Review. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2016 Sep;8(5):642-53. PMID: 26846457.

15. **Zamboni WC**. Pharmacokinetic and Pharmacodynamic Characterization of Nanotherapeutics, NCI Cancer Nanotechnology Plan 2015. https://www.cancer.gov/nano/research/plan/cananoplan-2015-complete.pdf.

16. Lucas A*, Madden A*, **Zamboni WC**. Formulation and physiological factors affecting the pharmacology of carrier-mediated agents. Expert Opin Drug Metab Toxicol. 2015;11(9):1419-33. PMID: 26173794.

17. O'Neal S, Lucas A*, Caron WP*, Song G*, Lay JC, **Zamboni WC**. Bidirectional Interaction Between Nanoparticles and Carrier-Mediated Agents and the Cells of the Mononuclear Phagocyte System. In: Dobrovolskaia M, editor. Immunological Properties of Engineered Nanomaterials. Second Edition. World Scientific. ISBN: 978-981-4699-16-7. 2015.

18. Petschauer JS, Madden AJ, Kirschbrown WP, Song G, **Zamboni WC**. The effects of nanoparticle drug loading on the pharmacokinetics of anticancer agents. Nanomedicine (Lond). 2015 Feb;10(3):447-63. doi: 10.2217/nnm.14.179. PubMed PMID:25707978.

19. Bartlett JA, Brewster M, Brown P, Cabral-Lilly D, Cruz CN, David R, EickhoffWM, Haubenreisser S, Jacobs A, Malinoski F, Morefield E, Nalubola R, Prud'homme RK, Sadrieh N, Sayes CM, Shahbazian H, Subbarao N, Tamarkin L, Tyner K, Uppoor R, Whittaker-Caulk M, **Zamboni W**. Summary report of PQRI Workshop on Nanomaterial in Drug Products: current experience and management of potential risks. AAPS J. 2015 Jan;17(1):44-64. doi: 10.1208/s12248-014-9701-9. Epub 2014 Nov 25. PubMed PMID:25421459; PubMed Central PMCID: PMC4287304.

20. Gabizon A, Bradbury M, Prabhakar U, **Zamboni W**, Libutti S, Grodzinski P. Cancer nanomedicines: closing the translational gap. Lancet. 2014 Dec 20;384(9961):2175-6. PMID: 25625382.

21. Song G, Petschauer JS, Madden AJ, **Zamboni WC**. Nanoparticles and the mononuclear phagocyte system: pharmacokinetics and applications for inflammatory diseases. Curr Rheumatol Rev. 2014;10(1):22-34. PubMed PMID: 25229496.

22. Smith M, Brown J, **Zamboni WC**, Walker N. Symposium Overview: From immunotoxicity to nanotherapy: the effects of nanomaterials on the immune system. Toxicol Sci. 2014 Apr;138(2):249-55. PMCID: PMC3988451.

23. Kam TC, **Zamboni WC**. Ovarian Cancer. In: Schwinghammer TL and Koehler JM, eds. Pharmacotherapy: A Patient-Focused Approach, 9th edition, McGraw-Hill, 2013.

24. Prabhakar U, Maeda H, Jain R, Sevick-Muraca E, **Zamboni W**, Barry S, Gabizon A, Grodzinski P, Blakey D. Challenges and key considerations of the enhanced permeability and retention effect (EPR) and nanomedicine drug delivery in oncology. Cancer Research. 2013;73(8):2412-7. PubMed Central: PMC3916009.

25. Kumar P*, Caron WP*, Song G*, Rawal S, **Zamboni WC**. Nanoparticle Effects on the Interaction with Cells of the Mononuclear Phagocytic System. In: Dobrovolskaia M, editor. Immunological Properties of Engineered Nanomaterials. First Edition. World Scientific 2013.

26. Caron WP*, Song G*, Kumar P*, Rawal S*, **Zamboni WC**. Pharmacokinetic and Pharmacodynamic Disposition of Carrier-Mediated Agents. Clin Pharmacol Ther. 91(5);802-12:2012.

27. **Zamboni WC**, Torchilin V, Patri A, Hrkach J, Lee R, Stern S, Nel A, Malghan S, Panaro N, Grodzinski P. Best Practices in Cancer Nanotechnology: Perspectives from NCI Nanotechnology Alliance. Clinical Cancer Research. Clin Cancer Res. 18(12);3229-41:2012. PubMed Central: PMC3916007.

28. Song G*, Wu H*, Yoshino K, **Zamboni WC**. Factors affecting the Pharmacokinetic and Pharmacodynamic Disposition of Liposomal Agents. J Liposomal Res. 22(3);177-92:2012.

29. **Zamboni WC** and La I*. Carrier-mediated and targeted cancer drug delivery. In: Armstrong D, editor. Oxidative Stress in Applied Basic Research and Clinical Practice. First Edition. Springer Science. Part 5, 427-452, 2012.

30. Combest AJ*, **Zamboni WC**. Use of microdialysis in preclinical and clinical development of anticancer agents. In Handbook of Anticancer Agents: Pharmacokinetics and Pharmacodynamics, 2nd Edition. Springer Science and Business Media, New York, NY; 2010, 2011.

31. La-Beck*, Walsh MD*, **Zamboni WC**. Ovarian Cancer. In: Schwinghammer TL and Koehler JM, eds. Pharmacotherapy: A Patient-Focused Approach, 8th edition, McGraw-Hill, 2011.

32. Sparreboom A and **Zamboni WC**. Camptothecin Analogues. In Chabner BA and Longo DL, editors. Cancer Chemotherapy and Biotherapy: Principles and Practice, Fourth Edition, Lippincott Williams & Wilkins, 2011.

33. **Zamboni WC**, Yoshino K, Formulation and Physiologic Factors Affecting the Pharmacokinetics and Pharmacodynamics of Liposomal Agents. Drug Delivery Systems. 25(1);58-70:2010.

34. La-Beck NM*, **Zamboni WC**. Pharmacokinetics and pharmacodynamics of nanoparticle anticancer agents. NCI Alliance for Nanotechnology in Cancer Bulletin 3(1);3-6:2009.

35. **Zamboni WC** and Tonda M. Ovarian Cancer. In: Dipro J, Talbert R, Matzke G, Posey L, editors. Pharmacotherapy: A Pathophysiological Approach, Seventh Edition, McGraw-Hill, 2008.

36. **Zamboni WC**. Concept and Clinical Evaluation of Nanoparticle and Nanosome Anticancer Agents. The Oncologist 13(3);248-60:2008.

37. Waddell JA, Adel NG, Almuete V, Ignoffo R, Medina PJ, Kuhn JC, Solimando DA, **Zamboni WC**. New treatments for the management of treatment-experienced breast cancer: examining the evidence. Advanced Studies in Pharmacy 4(13);2007.

38. **Zamboni WC**. Tumor Targeted Delivery of Drugs for the Treatment of Cancer. In: Prakash S, eds. Artificial Cell, Cell Engineering and Therapy, First Edition, Woodhead Publishing Limited, Cambridge, UK. 2007.

39. **Zamboni WC**. Liposomal, nanoparticle, conjugated formulations of anticancer agents. Invited Review. Clin Cancer Res 11(23);8230-4:2005.

40. Sparreboom A, **Zamboni WC**. Topoisomerase I Inhibitors. In Chabner BA and Longo DL, editors. Cancer Chemotherapy and Biotherapy: Principles and Practice, Fourth Edition, Lippincott Williams & Wilkins, 2005.

41. **Zamboni WC**, Jung L, Tonda M. Ovarian Cancer. In: Dipro J, Talbert R, Matzke G, Posey L, editors. Pharmacotherapy: A Pathophysiological Approach, Sixth Edition, McGraw-Hill, 2005.

42. **Zamboni WC**, Jung L, Tonda M. Ovarian Cancer. In: Schwinghammer T, eds. Pharmacotherapy: A Patient-Focused Approach, Sixth edition, McGraw-Hill, 2005.

43. **Zamboni WC**. Use of microdialysis in preclinical and clinical development. In: Figg WD, McLeod H, editors. Handbook of Pharmacokinetics and Pharmacodynamics of Anti-Cancer Drugs, First edition. Humana Press. 2004.

44. **Zamboni WC**. An overview of the pharmacokinetic disposition of PEG-GCSF. Pharmacotherapy, 23(8 Pt 2):9S-14S,2003.

45. **Zamboni WC** and Stewart CF. An overview of the pharmacokinetics disposition of darbapoetin. Pharmacotherapy. 22(9):133S-140S;2002.

46. Jung LJ* and **Zamboni WC**. Cellular, pharmacokinetic, and pharmacodynamic aspects of response to camptothecins: can we improve it? Drug Resistance Updates. 4(4):273-88;2001.

47. **Zamboni WC**, Jung L*, Tonda M. Ovarian Cancer. In: Schwinghammer T, Yee G, editors. Pharmacotherapy: A Patient-Focused Approach, Fifth edition. McGraw & Hill. 2001.

48. **Zamboni WC**, Jung L*, Tonda M. Ovarian Cancer. In: Dipro J, Talbert R, Matzke G, Posey L, editors. Pharmacotherapy: A Pathophysiological Approach, Fifth Edition. McGraw & Hill. 2001.

49. **Zamboni WC**, Tonda ME. New designs of clinical trials. Highlights in Oncology Practice, 18(1):2-7, 2000.

50. **Zamboni WC** and Trovato JA. Ovarian Cancer. In: Schwinghammer T, Yee G, editors. Pharmacotherapy: A Patient-Focused Approach, Second edition. Appleton & Lange. 1999.

51. **Zamboni WC** and Goldspiel B. Ovarian Cancer. In: Dipro J, Talbert R, Matzke G, Posey L, editors. Pharmacotherapy: A Pathophysiological Approach, Fourth Edition. 1999.

52. Stewart CF, **Zamboni WC**. Plasma Protein Binding of Chemotherapeutic Agents. In Grochow L, Ames M, editors. Pharmacokinetics and Pharmacodynamics of Anticancer Agents, Second Edition. 1998.

53. Masson E, **Zamboni WC**. Pharmacokinetic Optimization of Cancer Chemotherapy: Effect on Outcomes. Clin Pharmacokinetics. 32(4);324-343:1997.

54. **Zamboni WC**. Fruits of the Yew (Ovarian Cancer). In: Schwinghammer T, Yee G, editors. Pharmacotherapy: A Patient-Focused Approach, First edition. Appleton & Lange, 1996.

55. **Zamboni WC** and Goldspiel B. Ovarian Cancer. In: Dipro J, Talbert R, Hayes P, Matzke G, Posey L, editors. Pharmacotherapy: A Pathophysiological Approach, Third Edition. Appleton & Lange, 1996.

In Preparation:

None

Peer Reviewed Articles

Students and fellows under my direction are indicated by an asterick.

Published or In Press:

1. Mansfield AS, Yin JV, Bradbury P, Kwiatkowski D, Patel S, Bazhenova L, Forde P, Lou Y, Dizona P, Villaruz L, Arnold S, Khalil M, Kindler HL, Koczywas M, Pacheco J, Rolfo C, Xia B, Mikula E, Chen L*, Patel K*, Smith KER, Cao L, Shaprio G, Costello B, Adjei A, Sharon E, Moscow J, **Zamboni WC**, Hassan R. Phase 1/2 Randomized Trial of Anetumab Ravtansine and Pembrolizumab Compared to Pembrolizumab for Pleural Mesothelioma (NCI ETCTN 10107). Lung Cancer. 2024 Sep;195:107928. doi: 10.1016/j.lungcan.2024.107928. Epub 2024 Aug 13. PMID: 39197359; PMCID: PMC11416719.

2. Brickey WJ, Caudell DL, Macintyre AN, Olson JD, Dai Y, Li S, Dugan GO, Bourland JD, O'Donnell LM, Tooze JA, Huang G, Yang S, Guo H, French MN, Schorzman AN, **Zamboni WC**, Sempowski GD, Li Z, Owzar K, Chao NJ, Cline JM, Ting JPY. The TLR2/TLR6 ligand FSL-1 mitigates radiation-induced hematopoietic injury in mice and nonhuman primates. Proc Natl Acad Sci U S A. 2023 Dec 12;120(50):e2122178120. doi: 10.1073/pnas.2122178120. Epub 2023 Dec 5. PMID: 38051771; PMCID: PMC10723152.

3. Williams GR, Outlaw D, Harvey RD, Lichtman SM, **Zamboni WC**, Giri S. Chemotherapy dosing in older adults with cancer: One size does NOT fit all. J Geriatr Oncol. 2022 Aug 24:S1879-4068(22)00203-X. doi: 10.1016/j.jgo.2022.08.012. Epub ahead of print. PMID: 36030172.

4. Dahl DK, Whitesell AN, Sharma-Huynh P, Maturavongsadit P, Janusziewicz R, Fox RJ, Loznev HT, Button B, Schorzman AN, **Zamboni W**, Ban J, Montgomery SA, Carey ET, Rahima Benhabbour S. A mucoadhesive biodissolvable thin film for localized and rapid delivery of lidocaine for the treatment of vestibulodynia. Int J Pharm. 2022 Jan 25;612:121288. doi: 10.1016/j.ijpharm.2021.121288. Epub 2021 Nov 17. PMID: 34800616; PMCID: PMC8753993.

5. Arnold K, Wang Z, Lucas A, **Zamboni W**, Xu Y, Liu J. Investigation of the pharmacokinetic properties of synthetic heparan sulfate oligosaccharides. Glycobiology. 2022 Oct 14:cwac068. doi: 10.1093/glycob/cwac068. Epub ahead of print. PMID: 36239422.

6. Price L*, Rivera J, Madden A*, Herity L*, Piscitelli J*, Mageau S*, Santos D, Roques J, Midkiff B, Nikolaishvili-Feinberg N, Darr D, Chang S, **Zamboni W**. Minibeam radiation therapy enhanced tumor

delivery of PEGylated liposomal doxorubicin in a triple negative breast cancer mouse model. Resubmitted to Ther Adv in Med Oncol. 2021 Oct 29;13:17588359211053700. doi: 10.1177/17588359211053700. PMID: 34733359; PMCID: PMC8558804.

7. Benhabbour SR, Prasher A, Shrivastava R, Dahl D, Sharma-Huynh P, Pridgen T, Schorzman AN, Ban J*, **Zamboni WC**, Blikslager AT, Dellon ES. Steroid eluting esophageal-targeted drug delivery devices for treatment of eosinophilic esophagitis. Polymners. 2021 Feb 13;13(4):557. doi: 10.3390/polym13040557. PMID: 33668571; PMCID: PMC7917669.

8. Piha-Paul SA, Thein KZ, De Souza P, Kefford R, Gangadhar T, Smith C, Schuster S, **Zamboni WC**, Dees CE, Markman B. First-in-human, phase I/II study of CRLX301 in patients with advanced or metastatic solid malignancies. Invest New Drugs. 2021 Aug;39(4):1047-1056. doi: 10.1007/s10637-021-01081-x. Epub 2021 Feb 16. PMID: 33594602.

9. Duska L, O'Malley DM, Krasner C, Schilder RJ, Mathews C, Moore K, Thaker P, Miller A, Prudy C, Leyco AJ, Smith C, Mercier D, Tennant L, Kennedy E, Vahanian N, Lucas AT, **Zamboni WC**, Link C. A Phase Ib/II and pharmacokinetic study of EP0057 (formerly CRLX101) in combination with weekly paclitaxel in patients with recurrent or persistent epithelial ovarian, fallopian tube, or primary peritoneal cancer. Gynecol Oncol. Gynecol Oncol. 2021 Mar;160(3):688-695. doi: 10.1016/j.ygyno.2020.12.025. Epub 2020 Dec 31. PMID: 33390325.

10. Hwang D, Dismuke T, Rosen EP, Kagel JR, Lim C. **Zamboni WC**, Kabanov AV, Gershon TR, Sokolsky-Papkov M. Nanoparticle formulation improves the delivery and efficacy of vismodegib for brain tumor therapy in a GEMM of sonic hedgehog driven medulloblastoma. Nanomedicine. 2021 Feb;32:102345. doi: 10.1016/j.nano.2020.102345. Epub 2020 Nov 28. PMID: 33259959; PMCID: PMC8160025.

11. Price LSL*, Stern ST, Deal AM, Kabanov AV, **Zamboni WC**. A Reanalysis of Nanoparticle Tumor Delivery Using Classical Pharmacokinetic Metrics. Science Advances. 15 Jul 2020: Vol. 6, no. 29, eaay9249. DOI: 10.1126/sciadv. aay9249. PMID: 32832614 PMCID: PMC7439617.

12. Zhu J, Beechinor RJ, Thompson T, Schorzman AN, **Zamboni W**, Crona DJ, Weiner DL, Tarantino LM. Pharmacokinetic and pharmacodynamic analyses of cocaine and its metabolites in behaviorally divergent inbred mouse strains. Genes Brain Behav. 2020 May 8:e12666. doi: 10.1111/gbb.12666. PMID: 32383297.

13. Graham-Gurysh EG, Moore KM, Schorzman AN, Lee T*, **Zamboni WC**, Hingtgen SD, Bachelder EM, Ainslie KM. Tumor responsive and tunable polymeric platform for optimized delivery of paclitaxel to treat glioblastoma. ACS Appl Mater Interfaces. 2020 Apr 29;12(17):19345-19356. PMID: 32252517.

14. Parker CL, McSweeney MD, Lucas AT, Jacobs TM, Wadsworth D, **Zamboni WC**, Lai SK. Pre-targeted delivery of PEG-coated carriers to breast tumors using multivalent, bispecific antibody against polyethylene glycol and HER2. Nanomedicine. 2019 Oct; 21:102076. PMID: 31394261.

15. Salch SA, **Zamboni WC**, Zamboni BA, Eckel SF. Patterns and characteristics associated with the surface contamination of hazardous drugs in hospital pharmacies. Am J Health Syst Pharm. 2019 Apr 17;76(9):591-598. PMID: 31361828.

16. Taylor SE, Ruosha L, Petschauer JS*, Donovan H, Schorzman A, Razo J*, **Zamboni WC**, Edwards RP, Zorn KK. Phase I study of intravenous oxaliplatin and intraperitoneal docetaxel in recurrent ovarian cancer. Internat J of Gynecologic Cancer. 2019 Jan;29(1):147-152. PMID: 30640697.

17. Starling BR*, Kumar P*, Lucas A*, Barrow D, Farnan L, Song G*, Bae-Jump V, Gehrig P, Bensen J, **Zamboni WC**. Mononuclear phagocyte system function and nanoparticle pharmacology in obese and normal weight ovarian and endometrial cancer patients. Cancer Chemother Pharmacol. 2019 Jan;83(1):61-70. PMID: 30327876.

18. McSweeney MD, Wessler T, Price LSL*, Ciociola EC, Herity LB*, **Zamboni WC**, Forest MB, Coa Y, Lia SK. A minimal physiologically based pharmacokinetic model that predicts anti-PEG antibody-mediated clearance of PEGylated drugs in human and mouse. J Controlled Release. 2018 Aug 28; 284:171-178. PMID: 29879519.

19. Sanoff HK, Goldberg RM, Ivanova A, O'Reilly S, Kasbari SS, Kim RD, McDermott R, Moore DT, **Zamboni WC**, Grogan W, Cohn AL, Bekaii-Saab TS, Leonard G, Ryan T, Olowokure OO, Fernando NH, McCaffrey J, El-Rayes BF, Horgan AM, Sherrill GB, Yacoub GH, O"eil BH. Multi-center, randomized, double-blind phase II trial of FOLFIRI with regorafenib or placebo as second-line therapy for metastatic colorectal cancer. Cancer. 2018 Aug 1;124(15):3118-3126. PMID: 29905927.

20. Byrne J, Jajja MRN, O'Neill AT, Schorzman AN, Keeler AW*, Luft JC, **Zamboni WC**, DeSimone JM, Yeh JJ. Impact of formulation on the iontophoretic delivery of the FOLFIRINOX regimen for the treatment of pancreatic cancer. Cancer Chemother Pharmacol. 2018 Jun;81(6):991-998. PMID: 29603014.

21. Wu J, Frady LN, Bash RE, Cohen SM, Schorzman A, Su YT, Irvin DM, **Zamboni WC**, Wang X, Frye SV, Ewend MG, Sulman EP, Gilbert MR, Earp S, Miller CR. MerTK as a therapeutic target in glioblastoma. Neuro Oncol. 2018;10;20(1):92-102. PMID: 28605477.

22. **Zamboni WC**, Salch SA*, Cox J, Eckel S. It takes a village to raise awareness of and to address surface contamination of hazardous drugs. J Oncol Pharm Pract. 2017;23(7):558-560. PMID: 28791909.

23. McRee AJ, Marcom PK, Moore DT, **Zamboni WC**, Kornblum ZA*, Phipps R, Anders CK, Reeder-Hayes K, Carey LA, Perou CM, Dees EC. Phase I trial of the PI3K inhibitor buparlisib in combination with capecitabine in patients with metastatic breast cancer. Clin Breast Cancer. 2017. [Epub ahead of print]. PMID: 29153866.

24. Lucas AT*, Herity LB*, Kornblum ZA, Madden AJ*, Gabizon A, Layko D, Kabanov AV, Ajamie T, Bender DM, Kulanthaivel P, Sanchez-Felix MV, Havel HA, **Zamboni WC**. Pharmacokinetic and screening studies of the interaction between mononuclear phagocyte system and nanoparticle formulations and colloid forming drugs. Int J Pharm. 2017;526(1-2):443-454. PMID: 28473237.

25. Risselada M, Linder KE, Griffith E, Roberts BV*, Davidson G, **Zamboni WC**, Messenger KM. Pharmacokinetics and toxicity of subcutaneous administration of carboplatin in poloxamer 407 in a rodent model pilot study. PLOS ONE. 2017; 12(10):e0186018. PMID: 28982137.

26. Perry JL, Reuter KG, Luft JC, Pecot CV, **Zamboni WC,** DeSimone JM. Mediating passive tumor accumulation through particle size, tumor type and location. Nano Lett. 2017;17(5):2879-2886. PMID: 28287740.

27. Cox J, Speed V, Hasselwander T, O'Neil S, Sherwood C*, Eckel S, **Zamboni WC**. Development and evaluation of a novel product to remove surface contamination of hazardous drugs. J Oncol Pharm Pract. 2017;23(7):558-560. PMID: 28791909.

28. Madden AJ*, Oberhardt B, Lockney D, Santos C, Vennam P, Arney D, Franzen S, Lommel SA, Miller CR, Gerhig P, **Zamboni WC**. Pharmacokinetics and efficacy of doxorubicin loaded plant virus nanoparticles in preclinical models of cancer. Nanomedicine. 2017;12(20):2519-2532. PMID: 28952882.

29. Lucas AT*, White TF*, Deal AM, Herity LB*, Song G*, Santos CM, **Zamboni WC**. Profiling the relationship between tumor-associated macrophages and the pharmacokinetics of liposomal agents in preclinical murine models. Nanomedicine. 2017;13(2):471-482. PMID: 27720926.

30. Bowerman C, Bryne J, Chu K, Schorzman A, Keeler A*, Sherwood C, Perry J, Luft J, Darr D, Deal A, Napier M, **Zamboni WC**, Sharpless N, Perou C, DeSimone J. Docetaxel-loaded PLGA Nanoparticles Improve Efficacy in Taxane-Resistant Triple-Negative Breast Cancer. Nano Lett. 2017;17(1):242-248. PMID: 27966988.

31. Sambade M, Deal A, Schorzman A, Luft C, Bowerman C, Chu K, Karginova O, Van Swearingen A, **Zamboni WC**, DeSimone J, Anders CK. Efficacy, and pharmacokinetics of a modified acid-labile docetaxel-PRINT® nanoparticle formulation against non-small cell lung cancer brain metastases. Nanomedicine. 2016 Aug;11(15):1947-55. PMID: 27456556.

32. Patel NR, Piroyan A, Nack AH, Galati CA, McHugh M, Orosz S, Keeler AW*, David B, Sara O'Neal, **Zamboni WC**, Coleman TP. Design, synthesis, and characterization of folate-targeted platinum theranostics nanoemulsions for therapy and imaging of ovarian cancer. Mol Pharm. 2016;13(6):1996-2009. PMID: 27170232.

33. Song G*, Suzuki O, Santos CM, Wiltshire T, **Zamboni WC**. Gulp1 is associated with pharmacokinetics of PEGylated liposomal doxorubicin (PLD) in inbred mice strains. Nanomedicine. 2016;12(7):207-2017. PMID: 27288666.

34. Byrne JD, Jajja MRN, Schorzman AN, Keeler AW*, Luft JC, **Zamboni WC**, DeSimone JM, Yeh JJ. Iontophoretic Device Delivery for the Localized Treatment of Pancreatic Ductal Adenocarcinoma. PNAS. 2016;113(8):2200-5. PMID: 26858448.

35. Giovinazzo H*, Kumar P*, Sheik A, Ivanovic M, Walsh M*, Caron WP*, Kowalsky RJ, Song G*, Whitlow A, Clarke-Pearson DL, Brewster WR, Le LV, Bae-Jump V, Gehrig PA, **Zamboni WC**. Technetium-99m-Sulfur-Colloid as a Phenotypic Probe for the Pharmacokinetic and Pharmacodynamic disposition of PEGylated Liposomal Doxorubicin in Women with Recurrent Epithelial Ovarian Cancer. Cancer Chemother Pharmacol. 2016;77(3):565-73. PMID: 26822231.

36. Kai MP, Brighton HE, Shen TW, Fromen CA, Luft YE, Robbins GR, JC Luft, Keeler A*, Ting JPY, **Zamboni WC**, Bear JE, DeSimone. Tumor presence induces global immune changes and enhances nanoparticle clearance. ACS Nano. 2016;26;10(1):861-70. PMID: 26592524.

37. Lucas AT*, O'Neal SK, Santos CM, White TF*, **Zamboni WC**. A sensitive high performance liquid chromatography assay for the quantification of doxorubicin bound to DNA in tumor and tissues. J Pharm Biomed Anal. 2016; 119:122-9. PMID: 26678179.

38. Wallace BD, Roberts AB, Pollet RM, Ingle JD, Biernat K, Venkatesh MK, Guthrie L, O'Neal SK, Robinson SJ, Dollinger M, Figueroa E, McShane SR, Jin J, Frye SV, **Zamboni WC**, Pepe-Ranney C, Mani S, Kelly L, Redinbo MR. Structure, and Inhibition of GI Microbiome Targets that Alleviate Cancer Drug Toxicity. Chem Biol. 2015;22(9):1238-49. PMID: 26364932.

39. Song G*, Tarrant TK, Barrow DA, Santos CM, White TL*, Timoschenko RG, Hanna SK, Bae-Jump V, Gehrig P, **Zamboni WC**. Roles of chemokines CCL2 and CCL5 in the pharmacokinetics of PEGylated liposomal doxorubicin in vivo and in patients with recurrent epithelial ovarian cancer. Nanomedicine. 2015 Oct;11(7):1797-807. PMID: 26093057.

40. Taylor S, Li R, Petschauer JS*, Donovan H, O'Neal S, Keeler S*, **Zamboni WC**, Edwards RP, Zorn KK. Phase I Study of Intravenous (IV) Docetaxel and Intraperitoneal (IP) Oxaliplatin in Recurrent Ovarian and Fallopian Tube Cancer. Gynecol Oncol. 2015 Sep;138(3):548-53. PMID: 26111788.

41. Kai MP, Keeler AW*, Perry JL, Reuter KG, Luft JC, O'Neal SK, **Zamboni WC**, DeSimone JM. Evaluation of drug loading, pharmacokinetic behavior, and toxicity of a cisplatin-containing hydrogel nanoparticle. J Control Release. 2015 Apr 28; 204:70-7. PMID: 25744827.

42. Karginova O, Siegel MB, Adamo B, Deal A, Van Swearingen AED, Fienberg N, Parker J, Santos C, Darr D, Bash R, Sandison K*, **Zamboni WC**, Miller R, Anders CK. Efficacy of Carboplatin alone and in combination with ABT888 in BRCA-mutated and BRCA-wild-type Triple Negative Breast Cancer intracranial murine models. Mol Cancer Ther. 2015 Apr;14(4):920-30. PMID: 25824335.

43. Ganta S, Singh A, Kulkarni P, Keeler AW*, Piroyan A, Davis B, Ferris C, O'Neal, **Zamboni WC**, Amiji MM, Coleman TP. EGFR targeted combination therapy in a theranostic nanoemulsion for image-guided ovarian cancer therapy. Pharm Res. 2015 Mar 4. [Epub ahead of print] PubMed PMID: 25732960.

44. Wiltshire T, Ervin RB, Duan H, Bogue MA, **Zamboni WC**, Cook S, Chung W, Zou F, Tarantino LM. Initial locomotor sensitivity to cocaine varies widely among inbred mouse strains. Genes Brain Behav. 2015 Mar;14(3):271-80. PMID: 25727211. PMCID: PMC4692246.

45. Byrne JD, R Jajja MN, O'Neill AT, Bickford LR, Keeler AW*, Hyder N, Wagner K, Deal A, Little RE, Moffitt RA, Stack C, Nelson M, Brooks CR, Lee W, Luft JC, Napier ME, Darr D, Anders CK, Stack R,

Tepper JE, Wang AZ, **Zamboni WC**, Yeh JJ, DeSimone JM. Local iontophoretic administration of cytotoxic therapies to solid tumors. Sci Transl Med. 4;7(273):2015. PMID: 25653220.

46. Wu H, Infante JR, Keedy VL, Jones SF, Chan E, Bendell JC, Lee W, Kirschbrown WP, Ikeda S, Kodaira H, Rothenberg ML, Burris HA 3rd, **Zamboni WC**. Factors affecting the pharmacokinetics and pharmacodynamics of PEGylated liposomal irinotecan (IHL-305) in patients with advanced solid tumors. Int J Nanomedicine. 2015 Feb 10; 10:1201-9. doi: 10.2147/IJN.S62911. eCollection 2015. PubMed PMID: 25709442; PubMed Central PMCID: PMC4334335.

47. Song G*, Darr DB, Santos CM, Ross M, Valdivia A, Jordan JL*, Midkiff BR, Cohen S, Feinberg, Miller CR, Tarrant TK, Rogers AB, Dudley AC, Perou CM, **Zamboni WC**. Effects of tumor microenviroment on nanoparticle disposition and efficacy in triple negative breast cancer. Clinical Cancer Res, 2014;20(23):6083-95. PMID: 25231403.

48. Peng L, Schorzman AN, Benhabbour SR, Ma P, Madden AJ, **Zamboni WC**, Mumper RL. 2'-(2-bromohexadecanoyl)-paclitaxel conjugate nanoparticles for the treatment of non-small cell lung cancer in an orthotopic xenograft model. Int J Nanomedicine. 2014; 9:3601-10. PMID: 25114529.

49. Madden A*, Rawal S*, Chu K, Sandison K*, Schell R*, Feng L, Ma P, Deal A, Mumper R, DeSimone J, **Zamboni WC**. Evaluation of the efficiency of tumor and tissue delivery of carrier-mediated agents (CMA) and small molecule agents in mice using a novel pharmacokinetic metric: relative distribution index over time (RDI-OT). J Nanopart Res. 2014;16(11);2662.

50. Chu KS, Finniss M, Schorzman AS, Bowerman C, Luft CJ, Kuijer JL*, Napier ME, **Zamboni WC**, DeSimone JM. Particle replication in Nonwetting templates nanoparticles with tumor selective alkyl silyl ether docetaxel prodrug reduces toxicity. Nano Lett. 2014. 14(3):1472-6. PMID: 24552251.

51. Schell RF*, Sidone BJ*, Caron WP*, Walsh MD*, White TF*, **Zamboni WC**, Ramanathan RK, Zamboni WC. Meta-analysis of study design issues and pharmacokinetic variability of liposomal and non-liposomal anticancer agents in patients. Nanomedicine. 2014;10(1):109-117. PMID: 23891988.

52. Yang Q, Jones SW, Parker CL, **Zamboni WC**, Bear JE, Lai SK. Evading immune cells uptake and clearance requires PEG grafting at densities substantially exceeding the minimum for brush conformation. Mol. Pharmaceutics. 2014; 11(4): 1250-1258.

53. Ko EM, Lippmann Q, Caron WP, **Zamboni WC**, Gehrig PA. Clinical risk factors of PEGylated liposomal doxorubicin induced palmar plantar erythrodysesthesia in recurrent ovarian cancer patients. Gynecol Oncol. 2013;131(3):683-8. Epub 2013 Oct 4. PubMed PMID: 24096112.

54. Chu KS, Schorzman AN, Finniss MA, Bowerman CJ, Peng L, Luft JC, Madden A*, Wang AZ, **Zamboni WC**, DeSimone JM. Nanoparticle drug loading as a design parameter to improve docetaxel pharmacokinetics and efficacy. Biomaterials. 2013;34(33):8424-9. PMID: 23899444.

55. Wu H, Infante JR, Keedy VL, Jones SF, Chan E, Bendell JC, Lee W, **Zamboni WC**, Ikeda S, Kodaira H, Rothenberg ML, Burris HA 3rd, Zamboni WC. Population pharmacokinetics of PEGylated liposomal CPT-11 (IHL-305) in patients with advanced solid tumors. Eur J Clin Pharmacol. 2013 Dec;69(12):2073-81. Epub 2013 Aug 30. PubMed PMID: 23989300.

56. Zhang Y, Sadgrove MP, Sueda K, Yang YT, Pacyniak EK, Kagel JR, Braun BA, **Zamboni WC**, Mumper RJ, Jay M. Nonaqueous gel for the transdermal delivery of a DTPA penta-ethyl ester prodrug. AAPS J. 2013 Apr;15(2):523-32. Epub 2013 Feb 7. PubMed PMID: 23389812; PubMed Central PMCID: PMC3675732.

57. Caron WP*, Morgan KP*, Zamboni BA, **Zamboni WC**. A review of study designs and outcomes of phase I clinical studies of nanoparticle agents compared with small molecule anticancer agents. Clinical Cancer Res. 2013;19(12):3309-15. PMID: 23620407.

58. Usary J, Zhao W, Darr D, Roberts PJ, Liu M, Balletta L, Karginova O, Jordan J, Combest A*, Wu M*, Bridges A, Prat A, Cheang MCU, Herschkowitz JI, Rosen JM, **Zamboni WC**, Sharpless NE, Perou CM. Predicting drug responsiveness in human cancers using genetically engineered mice. Clinical Cancer Res. 2013;19(17):4889-99. PMID: 23780888.

59. Chu KS, Hasan W, Rawal S*, Walsh MD*, Enlow EM, Luft JC, Bridges AS, Coleman J*, Napier ME, **Zamboni WC**, DeSimone JM. Plasma, tumor and tissue pharmacokinetics of docetaxel delivered via nanoparticles of different sizes and shapes in mice bearing SKOV-3 human ovarian xenograft. Nanomedicine. 2013;9(5):686-93. PMID: 23219874. NIHMSID: NIHMS433583.

60. Caron WP*, Lay JC, Fong AM, La-Beck NM*, Kumar P*, Newman SE, Zamboni BA, Crona DJ, Clarke-Pearson DL, Brewster WR, Le LV, Bae-Jump V, Gehrig PA, **Zamboni WC**. Translational studies of phenotypic probes of the mononuclear phagocyte system and nanosomal pharmacology. J of Pharmacol Exp Ther. 2013;347(3):599-606. PMID: 24042160.

61. Anders CK, Adamo B, Rawal S*, Walsh MD*, Karginova O, Darr D, Deal AM, Santos C, Bash R, Hanna SK, Carey, LA, Miller CR, Sharpless N, Perou CM, **Zamboni WC**. Efficacy and pharmacokinetic disposition of PEGylated liposomal doxorubicin compared with non-liposomal doxorubicin in an intracranial breast cancer murine model. PLOS One. 2013;8(5):1-10. PMID: PMC3641071.

62. Combest AJ*, Roberts PJ, Dillon PJ, Habibi S, Eiseman JL, Strychor s, Hanna SK, Muller M, Brunner M, Ross CM, Sharpless NE, **Zamboni WC**. Genetically engineered cancer models, but not xenografts, faithfully predict anti-cancer drug exposure in melanoma. Oncologist 17(10);1303-16:2012. PubMed PMCID: PMC3481896.

63. Walsh MD, Hanna SK, Sen J, Rawal S, Cabral CB, Yurkovetskiy AV, Fram RJ, Lowinger TB, **Zamboni WC**. Pharmacokinetics and antitumor efficacy of XMT-1001, a novel, polymeric topoisomerase I inhibitor, in mice bearing HT-29 human colon carcinoma xenografts. Clin Cancer Res. 2012;18(9):2591-602. PubMed PMID: 22392910. PubMed PMID: 22392910.

64. Roberts PJ, Usary JE, Darr DB, Dillon PM, Johnson SM, Combest AJ*, Jin J, **Zamboni WC**, Perou CM, Sharpless NE. Combined PI3K/mTOR and MEK inhibition provides broad anti-tumor activity in faithful murine cancer models. Clin Cancer Res 18(19);5290-303:2012. PubMed PMID: 22872574.

65. Merkel TJ, Chen K, Jones SW, Pandya AA, Tian S, Napier ME, **Zamboni WC**, DeSimone JM. The effect of particle size on the biodistribution of low-modulus hydrogel PRINT particles. J Control Release. 162(1);37-44:2012. PubMed Central PMCID: PMC3416965.

66. Infante JR, Keedy V, Jones SF, **Zamboni WC**, Chan E, Bendell JC, Lee W, Wu H*, Ikeda S, Kodaira H, Rothenberg M, Burris HA. Phase I and pharmacokinetic study of IHL-305 (PEGylated liposomal irinotecan) in patients with advanced solid tumors. Cancer Chemother Pharmacol. 70(5);699-705:2012. PubMed PMID: 22941375.

67. Wu H*, Ramanathan RK*, Zamboni BA, Strychor S, Ramalingham S, Edwards RP, Friedland DM, Stoller RG, Belani CP, Maruca LJ*, Bang YJ, **Zamboni WC**. Mechanism-based pharmacokinetic-pharmacodynamic model characterizing the bi-directional interaction between PEGylated liposomal CKD-602 (S-CKD602) and monocytes in patients with advance malignancies. Int J of Nanomedicine. 7;5555-64:2012. PubMed PMCID: PMC3480239.

68. Walsh MD*, Hanna SK, Sen JM*, Rawal S*, Benson JD, Cabral CB, Yurkovetskiy A, Lowinger TB, Zamboni BA, **Zamboni WC**. Pharmacokinetics of XMT-1001, a novel polymeric prodrug of camptothecin, in mice bearing HT-29 human colon carcinoma xenografts. Clinical Cancer Res. 119(7);2591-602:2012. PubMed PMID: 22392910.

69. Roberts PJ, Bisi JE, Strum JC, Combest AJ*, **Zamboni WC**, Wong KK, Perou CM, Sharpless NE. Multiple roles of cyclin dependent kinase 4/6 in breast cancer therapy. Journal of National Cancer Inst. 104(6);476-87:2012. PubMed PMCID: PMC3309128.

70. La-Beck NM*, Zamboni BA, Gabizon A, Sidone BJ*, Edwards RP, Tzemach D, Schmeeda H, Sapir R, Amantea M, **Zamboni WC**. Factors affecting the pharmacokinetics of pegylated liposomal doxorubicin in patients. Cancer Chemotherapy Pharmacol. 69;43-50:2012. PubMed PMID: 21590446.

71. Wu H*, Ramanathan RK, Zamboni BA, Strychor S, Ramalingam S, Edwards RP, Friedland DM, Stoller RG, Belani CP, Maruca LJ*, Kim JK, Bang YJ, Lee HY, **Zamboni WC**. Population pharmacokinetics of PEGylated liposomal CKD-602 (S-CKD602) in patients with advanced malignancies. J Clin Pharmacol. 2012 Feb;52(2):180-94. doi: 10.1177/0091270010394851. PMID: 21233302.

72. Caron WP*, Clewell H, Dedrick R, Ramanathan R, Yu N, Tonda M, Schellens JH, Beijnen JH, **Zamboni WC**. Allometric scaling of pegylated liposomal anticancer agents. Journal of Pharmacokinetics and Pharmacodynamics. 38(5);653-69:2011. PubMed PMID: 21863380.

73. **Zamboni WC**, Combest AJ*, Bridges A, DeLoia j, Edwards R, Zorn KK, Walko CW, Kelley J. Pharmacologic and phenotypic study of docetaxel in patients with ovarian cancer. Cancer Chemotherapy and Pharmacol. 68(5);1255-62:2011. PubMed PMID: 21437702.

74. Merkel TJ, Jones SW, Herlihy KP, Kersey FR, Shields AR, Napier M, Luft JC, Wu H*, **Zamboni WC**, Wang AZ, Bear JE, DeSimone JM. Using mechano-biological mimicry to extend circulation times of hydrogel microparticles. PNAS 108(2);586-91:2011. PubMed PMCID: PMC3021010.

75. **Zamboni WC**, Maruca L*, Edwards RP, Strychor S, Lee S, Ahn SK, Friedland DM, Ramalingam S, Ramanathan RK. Bi-Directional pharmacodynamic interaction between pegylated liposomal CKD-602 (S-CKD602) and monocytes in patients with refractory solid tumors. J of Liposome Research, 21(2);158-65:2011. PubMed PMID: 20626314.

76. Rakhra-Burris TK, Auman JT, Deverka P, Dressler LG, Evans JP, Goldberg RM, Havener TM, Hoskins JM, Jonas DE, Long KM, Motsinger-Reif AA, Irvin WJ, Richards KL, Roederer MW, Valgus JM, Riper M, Vernon JA, **Zamboni WC**, Wagner MJ, Walko CM, Weck KE, Wiltshire T, McLeod HL. Institutional profile. UNC Institute for Pharmacogenomics and Individualized Therapy: interdisciplinary research for individual care. Pharmacogenomics. 11(1);13-21:2010. PubMed PMID: 20017668.

77. **Zamboni WC**, Maruca L, Strychor S, Zamboni BA, Ramalingam S, Friedland DM, Edwards RP, Stoller RG, Belani CP, Ramanathan RK. Pharmacokinetic study of pegylated liposomal CKD-602 (S-CKD602) in patients with solid tumors. Clinical Pharmacol Ther. 86(5);519-26:2010. PubMed PMCID: PMC3428134.

78. **Zamboni WC**, Eiseman JL, Strychor S, Rice PM, Joseph E, Zamboni BA, Donnelly MK*, Shurer J*, Parise RA, Tonda ME, Yu NY, Engber C, Basse PH. Tumor disposition of pegylated liposomal CKD-602 (S-CKD602) and the reticuloendothelial system in preclinical tumor models. J of Liposome Research 21(1);70-80:2010. PubMed PMID: 20528623.

79. Tuscano J, Martin S, Ma YP, **Zamboni WC**, O'Donnell R. Efficacy, biodistribution, and pharmacokinetics of CD22-targareted pegylated liposomal doxorubicin in a B-cell non-Hodgkin's lymphoma xenograft mouse model. Clinical Cancer Res. 16(10);2760-8:2010. PubMed PMID: 20460479.

80. O'Donnell RT, Martin SM, Ma Y, **Zamboni WC**, Tuscano JM. Development and characterization of CD22-targeted pegylated liposomal doxorubicin (IL-PLD). Invest New Drugs. 28(3);260-7:2010. PubMed PMCID: PMC2850518.

81. Wonganan P, **Zamboni WC**, Strychor S, Dekker JD, Croyle MA. Drug-virus interaction: effect of administration of recombinant adenovirus on pharmacokinetics of docetaxel in a rat model. Cancer Gene Therapy 16;405-414:2009. PubMed PMID: 19110543.

82. **Zamboni WC**, Strychor S, Maruca L, Ramalingam S, Zamboni BA, Wu H, Friedland DM, Edwards RP, Stoller RG, Belani CP, Ramanathan RK. Pharmacokinetic study of pegylated liposomal CKD-602 (S-CKD602) in patients with advanced malignancies. Clin Pharmacol Ther. 2009;86(5):519-26. PubMed PMID: 19675541.

83. **Zamboni WC**, Ramalingam S, Friedland DM, Edwards RP, Stoller RG, Strychor S, Maruca L*, Zamboni BA, Belani CP, Ramanathan RK. Phase I and pharmacokinetic study of STEALTH liposomal CKD-602 (S-CKD602) in patients with advanced solid tumors. Clin Cancer Res. 15(4);1466-72:2009. PubMed PMID: 19190127.

84. Florian JA*, **Zamboni WC**, Eiseman JL, Strychor S, Joseph E, Parise RA, Egorin MJ, Parker RS. A physiologically based pharmacokinetic model for docetaxel distribution in SCID mice bearing SKOV-3 ovarian tumor xenografts. Submitted to the Journal of Pharmacokinetics and Pharmacodynamics, Dec 2009.

85. Sivak WN*, Zhang J, Petoud S, **Zamboni WC**, Beckman, EJ. Incorporation of cationic and anionic constituents accelerates the release of DB-67 from LDI-glycerol polyurethane implants. Submitted to Journal of Controlled Released in Dec 2009.

86. Kimball KJ, Numnum TM, Kirby TO, **Zamboni WC**, Estes JM, Barnes MN, Matei DE, Koch KM, Alvarez RD. A phase I study of lapatinib in combination with carboplatin in women with platinum sensitive recurrent ovarian cancer. Gynecol Oncol 111(1);95-101:2008. PubMed PMID: 18692224.

87. **Zamboni WC**, Jung L*, Strychor S, Joseph E, Zamboni BA, Fetterman SA*, Sidone BJ*, Burke T, Curran D, Eiseman JL. Plasma and tissue disposition of non-liposomal DB-67 and liposomal DB-67 in SCID mice. Invest New Drugs 26(5);399-406:2008. PubMed PMID: 18246299.

88. Sivak WN*, Pollack IF, Petoud S, **Zamboni W**C, Zhang J, Beckman EJ. Catalyst-dependent drug loading of LDI-glycerol polyurethane foams leads to differing controlled release profiles. Acta Biomater 4(5);1263-74:2008. PubMed PMID: 18440884.

89. Sivak WN*, Pollack IF, Petoud S, **Zamboni WC**, Zhang J, Beckman EJ. LDI-glcerol polyurethane implants exhibit controlled release of DB-67 and anti-tumour acitivity against malignant gliomas. Acta Biomater 4(4);852-62:2008. PubMed PMID:18440882.

90. **Zamboni WC**, Strychor S, Joseph E, Parise R, Egorin MJ, Eiseman JL. Tumor, tissue, and plasma pharmacokinetic study of docetaxel in combination with 9-nitrocamptothecin in mice bearing SKOV3 human ovarian xenografts. Cancer Chemother Pharmacol 62(3);417-26:2008. PubMed PMID: 17957368.

91. **Zamboni WC**, Strychor S, Joseph E, Walsh DR*, Parise RA, Tonda ME, Yu NY, Engber C, Eiseman JL. Plasma, tumor, and tissue disposition of STEALTH liposomal CKD-602 (S-CKD602) and Non-liposomal CKD-602 in mice bearing A375 human melanoma xenografts. Clin Cancer Res 13(23):7217-23:2007. PubMed PMID: 18056203.

92. Loos WJ, **Zamboni WC**, Engels FK, Bruijn P, Lam MH, Verweij J, Wiemer EAC. Pitfalls of the use of microdialysis in clinical oncology: experience with taxanes. J Pharm Biomed Anal 45(2);288-94:2007. PubMed PMID: 17804188.

93. Deloia JA, **Zamboni WC**, Jones J, Strychor S, Gallion HH. Variable expression of taxane-metabolizing enzymes in ovarian tumors: a potentially novel mechanism of taxane resistance. Gynecol Oncol 108(2);355-60:2007. PubMed PMID: 18063021.

94. **Zamboni WC**, Strychor S, Joseph E, Walsh DR, Zamboni BA, Parise RA, Tonda ME, Yu NY, Engbers C, Eiseman JL. Plasma, tumor, and tissue disposition of STEALTH liposomal CKD-602 (S-CKD602) and nonliposomal CKD-602 in mice bearing A375 human melanoma xenografts. Clin Cancer Res. 2007;13(23):7217-23. PubMed PMID: 18056203. PubMed PMID: 18056203.

95. Thomas SM, Ogagan MJ, Freilino M, Wentzel AL, Gooding WE, Strychor S, Walsh DR*, Grandis JR, Zamboni WC. Systemic administration of epidermal growth factor receptor antisense oligonucleotide in combination with docetaxel as a treatment modality for squamous cell carcinoma of the head and neck. Mol Pharmacol 73(3)627-38:2007. PubMed PMID: 18025070.

96. Akhavan A, McHugh KH, Guruli G, Bies RR, **Zamboni WC**, Strychor S, Nelson JB, Pflug BR. Endothelin receptor A blockade enhances taxane effects in prostate cancer. Neoplasia 8(9);725-32:2006. PubMed PMID: 16984730.

97. Patel H, Stoller R, Auber M, Potter D, Cali C, **Zamboni WC**, Kiefer G, Matin K, Schmotzer A, Ramanathan RK. Phase II study of rubitecan, an oral camptothecin in patients with advanced colorectal cancer who have failed previous 5-fluorouracil based chemotherapy. Invest New Drugs 24(4);359-363:2006. PubMed PMID: 16525767.

98. **Zamboni WC**, Ramanathan RK, Mani S, McLeod HL, Potter DM, Maruca LJ*, Strychor S, Jung LL, Parise RA, Marsh S. Disposition of 9-nitrocamptothecin and its 9-aminocamptothecin metabolite in relation to ABC Genotypes. Invest New Drugs 24(5);393-401:2006. PubMed PMID: 16505951.

99. Brown DB, Cai SR, Fundakowski CE, **Zamboni WC**, Strychor S, McLeod HL. Pharmacokinetics after endovascular lung perfusion with cisplatin. J Vasc Interv Radiol. 17;883-888:2006. PubMed PMID: 16687755.

100. **Zamboni WC**, Goel S, Iqbal T, Parise RA, Strychor S, Repinski TVW*, Egorin MJ, Mani S. Pharmacokinetic study evaluating the effect of food on the disposition of 9-nitrocamptothecin and its 9-aminocamptothecin metabolite in patients with solid tumors. Cancer Chemother Pharmacol. 57(5);631-9:2006. PubMed PMID: 16205924.

101. Fakih MG, Creaven PJ, Ramnath N, Trump D, Javle M, Strychor S, Repinski TVW, Zamboni BA, Schwarz JK, French RA, **Zamboni WC**. Phase I and Pharmacokinetic Study of Weekly Docetaxel, Cisplatin, and Daily Capecitabine in Patients with Advanced Solid Tumors. Clinical Cancer Research. 2005;11(16):5942-9. doi: 10.1158/1078-0432.ccr-05-0116. PubMed PMID: 16115937.

102. Gillenwater HH, McCune JS, Lindley C, Stewart CF, Faucette S, **Zamboni WC**, Kirstein MN, Stacy Shord, Donahue A, Moore D, Socinski MA. A phase I trial defining the maximum tolerated systemic exposure of topotecan in combination with carboplatin and etoposide in extensive stage small cell lung cancer. Cancer Investigations. 23:511-19;2005. PubMed PMID: 16203659.

103. Fakih MG, Ramanath N, Javie MM, Schwarz JK, French RE, Regal LL, Ramanathan RK, Zamboni BA, Strychor S, Repinski TVW*, Gorenflo RK, Creaven PJ, **Zamboni WC**. A phase I and pharmacokinetic study of weekly docetaxel, cisplatin, and daily capecitabine in patients with advanced solid tumors. Clinical Cancer Research. 11(16):5942-9;2005. PubMed PMID: 16115937.

104. Harrold JM, Eiseman JL, Joseph E, Strychor S, **Zamboni WC**, Parker RS. Control-relevant modeling of the antitumor effects of 9-nitrocamptothecin in SCID mice bearing HT29 human colon xenografts. J Pharmacokinet and Pharmacodyn. 32(1);65-83:2005. PubMed PMID: 16205839.

105. Posey J, Zhang R, Delgrosso A, Hamilton J, Carpenter M, Freda T*, **Zamboni WC**. A Phase I Dose Escalation in Sequencing study of Docetaxel and Continuous Infusion Topotecan in Patients with Advanced Malignancies. Cancer Chemother Pharmacol 56(2):182-8, 2005. PubMed PMID: 15838660.

106. Ramanathan RK, Ramalingam S, Egorin MJ, Belani CP, Potter DM, Fakih M, Jung LL*, Strychor S, Jacobs SA, Friedland DM, Shin DM, Chatta GS, Tutchko S, **Zamboni WC**. Phase I study of weekly (day 1 and 8) docetaxel in combination with capecitabine in patients with advanced solid malignancies. Cancer Chemother Pharmacol 55(4):354-60, 2005. PubMed PMID: 15723261.

107. **Zamboni WC**, Hamburger DR, Jung LL*, Jin R, Joseph E, Strychor S, Sun SL, Egorin MJ, Eiseman JL. Relationship between systemic exposure of 9-nitrocamptothecin and its 9-aminocamptothecin metabolite and tumor response in human colon tumor xenografts. Clin Cancer Res 11(13):4867-74, 2005. PubMed PMID: 16000585.

108. **Zamboni WC**, Gervais AC*, Schellen JHM, Delauter BJ*, Egorin MJ, Zuhowski EG, Pluim D, Hamburger DR*, Working PK, Eiseman JL. Disposition of platinum in B16 murine melanoma tumors after administration of cisplatin & pegylated liposomal-cisplatin formulations (SPI-077 & SPI-077 B103). Cancer Chemotherapy and Pharmacology, 53:329-336;2004. PubMed PMID: 14673619.

109. Brown DB, Ma MK, Battafarano RJ, Naidu S, Pluim D, **Zamboni WC**, McLeod HL. Endovascular lung perfusion using high-dose cisplatin: uptake of DNA adduct formation in an animal model. Oncol Rep. 11(1):237-43;2004. PubMed PMID: 14654932.

110. Ramanathan RK, Hwang JJ, **Zamboni WC**, Sinicrope FA, Safran H, Earle M, Brufsky A, Evans T, Troetschel M, Walko C*, Day R, Finkelstein S. Low expression of HER-2/neu in advanced colorectal cancer limits the usefulness of trastuzumab (Herceptin) and irinotecan therapy. A phase II trial. Cancer Invest 22(6):858-65, 2004. PubMed PMID: 15641483.

111. **Zamboni WC**, Jung LL*, Egorin MJ, Jin R, Wong MMW, Potter D, Vozniak M*, Sun S, Trump DL, Fakih M, Ramanathan R. Phase I and Pharmacologic studies of intermittently administered 9-nitrocamptothecin. Clinical Cancer Research 1;10(15):5058-64, 2004. PubMed PMID: 15297407.

112. Jung LL*, Ramanathan R, Egorin MJ, Jin R, Wong MMW, Potter D, Strychor S, Sun S, Trump DL, Fakih M, **Zamboni WC**. Pharmacokinetics studies of 9-nitrocamptothecin on intermittent and continuous schedules in patients with advanced cancer. Cancer Chemotherapy and Pharmacology. Cancer Chemother Pharmacol. 54(6):487-96, 2004. PubMed PMID: 15322760.

113. Stewart CF, Iacono LC, Chintagumpala M, Kellie SJ, Ashley D, **Zamboni WC**, Kirstein MN, Fouladi M, Seele LG, Wallace D, Houghton PJ, Gajjar A. Results of a phase II upfront window of pharmacokinetically guided topotecan in high-risk medulloblastoma and supratentorial primitive neuroectodermal tumor (PNET). Journal of Clinically Oncology 15;22(16):3357-65, 2004. PubMed PMID: 15310781.

114. Ramanathan RK, Hwang JJ, **Zamboni WC**, Sinicrope F, Finkelstein S, Safran H, Wong MK, Earle M, Brufsky A, Troetschel M, Walko C, Day R, Chen HX, Sydney F. Low over expression of HER-2/Neu in advanced colorectal cancer limits the usefulness of trastuzumab (Herceptin) and irinotecan as therapy: A phase II trial. Cancer Invest. 22(6):858-65, 2004. PubMed PMID: 15641483.

115. Goel S, Bulgaru A, Hochster H, Wadler S, **Zamboni WC**, Egorin M, Ivy P, Leibes L, Muggia F, Lockwood G, Harvey E, Renshaw G, Mani S. Phase I clinical study of infusional 5-fluorouracil with oxaliplatin and gemcitabine (FOG regimen) in patients with solid tumors. Ann Oncol. 14(11):1682-7,2003. PubMed PMID: 14581279.

116. Santana VM, **Zamboni WC**, Kirstein MN, Tan M, Liu T, Gajjar A, Houghton PJ, Stewart CF. A pilot study of protracted topotecan dosing using a pharmacokinetically guided dosing approach in children with solid tumors. Clinical Cancer Res. 9:633-640;2003. PubMed PMID: 12576429.

117. Parise RA, Ramanathan RK, **Zamboni WC**, Egorin MJ. A sensitive high-performance liquid chromatography-mass spectrometry assay for quantitation of docetaxel and paclitaxel in plasma. J Chromatography, Analytical Technology, & Life Sci, 783(1):231-236;2003. PubMed PMID: 12450543.

118. **Zamboni WC**, Gervias AC, Egorin MJ, Schellens JHM, Hamburger DR, Delauter BJ, Grim A, Zuhowski EG, Joseph E, Pluim D, Potter DM, Eiseman JL. Inter- and intra-tumoral disposition of platinum in solid tumors after administration of cisplatin. Clinical Cancer Research, 8(9):2992-2999;2002. PubMed PMID: 12231546.

119. Herrington JD, Figueroa JA, Kirstein MN, **Zamboni WC**, Stewart CF. Effect of hemodialysis on topotecan disposition in a patient with severe renal dysfunction. Cancer Chemotherapy and Pharmacology, 47(1):89-93;2001. PubMed PMID: 11221968.

120. **Zamboni WC**, D'Argenio, D, Stewart CF, MacVittie T, Delauter B*, Potter DP, Farese AM, Kubat N*, Tubergen D, Egorin MJ. Pharmacodynamic model of topotecan induced time-course of neutropenia. Clinical Cancer Research, 7:2301-2308, 2001. PubMed PMID: 11489805.

121. **Zamboni WC**, Luftner D, Possinger D, Schweigert M, Sezer O, Dobson J, Egorin M. Increasing topotecan infusion from 30-minutes to 4-hours infusions prolongs the duration of exposure in the cerebrospinal fluid. Annuals of Oncology, 12:119-122, 2001. PubMed PMID: 11249038.

122. Tkaczuk K, **Zamboni WC**, Tait N, Meisenbery B, Doyle LA, Hausner P, Egorin M, Van Echo D. Phase I study of docetaxel and topotecan in patients with solid tumor malignancies. Cancer Chemotherapy and Pharmacology, 46(6):442-8, 2000. PubMed PMID: 11138457.

123. **Zamboni WC**, Egorin M, Van Echo D, Day R, Doyle LA, Nemieboka N, Dobson J, Tait N, Tkaczuk K. Pretreatment with topotecan decreases docetaxel clearance and increases toxicity. Journal of Clinical Oncology, 18(17):3288-3294, 2000.

124. Delauter BJ*, Ramanathan RK, Stover LL, Zuhowski EG, Egorin MJ, Plunkett WK, **Zamboni WC**. Pharmacokinetics of gemcitabine and 2'-2'-difluorodeoxyuridine in a patient with ascites. Pharmacotherapy, 20(10):1204-1207, 2000. PubMed PMID: 11034044.

125. Ma M, **Zamboni WC**, Furman WL, Santana VM, Gajjar A, Houghton PJ, Stewart CF. Pharmacokinetics of Irinotecan and its active metabolite SN-38 in children with recurrent solid tumors after protracted low

dose intravenous administration. Clinical Cancer Research, 6:813-819, 2000. PubMed PMID: 10741701.

126. Furman WL, Stewart CF, Poquette CA, Pratt CB, Santana VM, **Zamboni WC**, Bowman LC, Ma MK, Hoffer FA, Meyer WH, Pappo AS, Walter AW, Houghton PJ. Direct translation of a protracted irinotecan schedule from xenograft model to phase I trial in children. Journal of Clinical Oncology, 17:1815-1824,1999. PubMed PMID: 10561220.

127. **Zamboni WC**, Houghton PJ, Danks MK, Hulstein JL, Kristein M, Walsh J, Cheshire PJ, Stewart CF. Relationship between tumor extracellular fluid exposure to topotecan and tumor response in human neuroblastoma xenografts and cells. Journal of Cancer Chemotherapy and Pharmacology, 43(4):269-276, 1999. PubMed PMID: 10071976.

128. **Zamboni WC**, Bowman LC, Santana VM, Houghton PJ, Pratt CB, Gajjar AJ, Pappa AS, Stewart CF. Interpatient Variability in Bioavailability and Pharmacokinetics of Oral Topotecan in Children with Relapsed Solid Tumors. Cancer Chemotherapy and Pharmacology, 43(6):454-460; 1999. PubMed PMID: 10321504.

129. **Zamboni WC**, Gajjar AJ, Houghton PJ, Mandrell TD, Einhaus SL, Danks MK, Rogers WP, Heideman RL, Stewart CF. A topotecan 4-hour intravenous infusion achieves cytotoxic exposure throughout the neuraxis in the nonhuman primate model: implications for the treatment of children with metastatic medulloblastoma. Clinical Cancer Research, 4:2537-2544, 1998. PubMed PMID: 9796988.

130. **Zamboni WC**, Gajjar AJ, Heideman RL, Biejnen J, Rosing H, Houghton PJ, Stewart CF. Phenytoin alters the disposition of topotecan and N-desmethyl metabolite in a patient with medulloblastoma. Clinical Cancer Research, 4:783-789, 1998. PubMed PMID: 9533548.

131. **Zamboni WC**, Stewart CF, Cheshire PJ, Richmond L, Luo X, McGovern P, Houghton JA, Houghton PJ. Studies of the Efficacy and Pharmacology of Irinotecan Against Human Colon Tumor Xenograft Models. Clinical Cancer Research, 4:743-753; 1998. PubMed PMID: 9533544.

132. **Zamboni WC**, Stewart CF, Thompson J, Santana V, Cheshire PJ, Richmond LB, Lui X, Houghton JA, Houghton PJ. The Relationship between Topotecan Systemic Exposure and Tumor Response in Human Neuroblastoma Xenografts. Journal of National Cancer Institute, 90(7):505-511, 1998. PubMed PMID: 9539245.

133. **Zamboni WC**, Houghton PJ, Crom WR, Thompson J, Cheshire PJ, Richmond LB, Stewart CF. Altered Irinotecan and SN-38 Pharmacokinetic Disposition in Mice Bearing Human Neuroblastoma Xenografts. Clinical Cancer Reseach, 4:455-462; 1998. PubMed PMID: 9516936.

134. **Zamboni WC**, Houghton PJ, Johnson RK, Hulstein JL, Crom WR, Cheshire PJ, Stewart CF. Probenecid Alters Topotecan Systemic and Renal Disposition by Inhibiting Renal Tubular Secretion. Journal of Pharmacology and Experimental Therapeutics, 284(1):89-94; 1998. PubMed PMID: 9435165.

135. Saylors RL, Stewart CF, **Zamboni WC**, Wall D, Bell B, Vietti TJ. Phase I Study of Topotecan in Combination with Cyclophosphamide in Pediatric Patients with Malignant Solid Tumors: A Pediatric Oncology Group Study. Journal of Clinical Oncology, 16:945-952, 1998. PubMed PMID: 9508177.

136. Thompson J, Pratt CB, Stewart CF, Avery L, Bowman L, **Zamboni WC**, Pappo A. Phase I Study of DMP-840 in Pediatric Patients with Refractory Solid Tumors Invest New Drugs. 16(1);45-49:1998. PubMed PMID: 9740543.

137. Thompson J, **Zamboni WC**, Cheshire P, Lutz L, Luo X, Houghton J, Stewart C, Houghton P. Efficacy of Systemic Administration of Irinotecan Against Neuroblastoma Xenografts. Clinical Cancer Research. 3(3);423-431:1998. PubMed PMID: 9815701.

138. Thompson J, **Zamboni WC**, Cheshire P, Richmond L, Luo X, Houghton J, Stewart C, Houghton P. Efficacy of Oral Irinotecan Against Neuroblastoma Xenografts. Journal of Anti-Cancer Drugs. 8:313-322;1997. PubMed PMID: 9180383.

139. Stewart CF, **Zamboni WC**, Crom WR, Houghton PJ. Disposition of Irinotecan and SN-38 Following Oral and Intravenous Irinotecan Dosing in Mice. Cancer Chemother Pharmacol. 40: 259-265; 1997. PubMed PMID: 9219511.

140. Tubergen DG, Stewart CF, Pratt CB, **Zamboni WC**, Santana VM, Dryer ZA, Kurtzberg J, Bell B, Grier H, Vietti TJ. Phase I Trial and Pharmacokinetic (PK) and Pharmacodynamic (PD) Study of Topotecan Using a Five-Day Course in Children With Refractory Solid Tumors: A Pediatric Oncology Group Study. J Pediatr Hematol Oncol 18(4): 352-61, 1996. PubMed PMID: 8888741.

141. Houghton PJ, Stewart CF, **Zamboni WC**, Thompson J, Danks MK, Houghton JA. Schedule dependent efficacy of camptothecins in models of human cancer. Ann N Y Acad Sci 803: 188-201, 1996. PubMed PMID: 8993512.

142. Stewart CF, **Zamboni WC**, Crom WR, Gajjar A, Heideman RL, Furman WL, Meyer WH, Houghton PJ, Pratt CB. Topoisomerase I interactive drugs in children with cancer. Investigational New Drugs 14:37-47; 1996. PubMed PMID: 8880392.

<u>Submitted or Resubmitted:</u>

1. Chen Li*, Lucas AT, Mansfield AS, Lheureux S, O'Connor C*, Zamboni BA, Patel K*, McKee T, Moscow J, **Zamboni WC**. Evaluation of Innate Immune System Biomarkers, Body Habitus, and Sex on the Pharmacokinetics and Pharmacodynamics of Anetumab Ravtansine in Patients With Cancer. Submitted to Clinical Pharmacology and Therapeutics, Aug 2024.

2. Alqaisi HA, Cohn DE, Cherm MJY, Duska LR, Jewell A, Corr B, Winer IS, Girda E, Crispens MA, Dhani NC, Madariaga AU, Grant R, Malaguti M, Lee C, Bowering V, Wong, H, Poothullil A, Speers V, Wang L, Bedard PL, Brady C, Nixon A, Chen Li*, O'Connor C*, **Zamboni W**, Moscow J, Oza AM, Lheureux S. A randomized phase II study of bevacizumab with weekly anetumab ravtansine or weekly paclitaxel in platinum-resistant/refractory high grade ovarian cancer (NCI trial#10150). Submitted to Clin Cancer Res in Aug 2024.

3. Lucas AT, Price LSL*, Santos CM, Perou C, Kabanov AV, **Zamboni WC**. Fibroblast-mediated increase in tumor density is associated with reduced nanoparticle tumor delivery and efficacy. Submitted to Science Advances, March 2024.

<u>In Preparation</u>:

4. Thakkar E*, Turner D, Santana V, Li J, Zamboni BA, Stewart C, **Zamboni WC**. The effect of body habitus on the pharmacokinetics of bevacizumab in pediatric and adults patients with refractory solid tumors. (Plan to submit to Clinical Pharmacology and Therapeutics).

5. **Zamboni WC**, Taft-Benz SA, Lucas AT, Moseley C, Zamboni BA, Heise M. COVID-19 infection alters the innate immune system and the pharmacokinetics of PEG-liposomal doxorubicin in mice.

6. Ghamande SA, Odunsi K, Combest AJ*, Walko CW, Hoskins J, Bridges A, Lele S, Macfee M, Rodabaugh K, Thomas B, McLeod H, **Zamboni WC**. A Phase II, pharmacologic and pharmacogenetic study of weekly docetaxel in patients with platinum resistant ovarian cancer.

7. Hwang JJ, **Zamboni WC**, Malik S, Hansen N, Strychor S, Zamboni BA, Sidone BJ*, Marshall JL. Phase I and pharmacokinetic study of weekly docetaxel and oxaliplatin in patients with advanced solid tumors.

8. Lucas AT, Santos CM, Kabanov AV, **Zamboni WC**, Bronich TK. Pharmacology of variably-loaded tri-block co-polymer formulations of cisplatin in a genetically engineered mouse model of triple negative breast cancer. (Plan to submit to Journal of Controlled Release).

1. Lucas AT, Beaudoin JJ*, Herity L*, Razo*, Sketch M, Price LSL*, **Zamboni WC**. Pharmacokinetic and allometric scaling studies of nanoparticle formulations of anthracyclines. Submitted to Journal of Pharmacokinetics and Pharmacodynamics, Dec 2023.

2. Madden AJ*, Price LSL*, Sandison KL*, White TF*, Santos CM, O'Neil S, Fitch RM, McGee W, Miller R, **Zamboni WC**. The effect of dose of actively and passively targeted PEGylated liposomal formulations of cisplatin on tumor delivery and interaction with tumor associated macrophages. Submitted to Nanomedicine NBM, July 202.

Abstracts and Scientific Presentations At Meetings

Students and fellows under my direction are indicated by an asterisk.

Published or Accepted:

1. Chen Li*, Lucas AT, Mansfield AS, Lheureux S, Patel K*, O'Connor C*, Hassan R, Moscow J, Zamboni WC. Evaluation of Innate Immune System Biomarkers, Body Habitus, and Sex on the Pharmacokinetics and Pharmacodynamics of Anetumab Ravtansine in Patients With Cancer. 2024 Annual Meeting of the American College of Clinical Pharmacology.

2. Williams GR, Al-Obaidi M, Rower J, Harmon C, Dai C, Acosta E, Giri S, **Zamboni W**, Lucas AT, Shachar SS, Gbolahan O, Meyerhardt J, Caan B, Bhatia S. Does Oxaliplatin Pharmacokinetics (PKs) explain the association between Body Composition and Chemotoxicity Risk in older patients with gastrointestinal (GI) Cancers. ASCO 2022.

3. Johannessen L, Hu S, Ke N, D'Ippolito A, Rajagopal N, Savinainen A, **Zamboni W**, Hodgson G. Preclinical evaluation of PK, PD, and anti-tumor activity of the oral, non-covalent, potent and highly selective CDK7 inhibitor, SY-5609, provides rationale for clinical development in multiple solid tumor indications. AACR-NCI-EORTC 2019 #C091.

4. Starling BR, Kumar P, Lucas AT, Barrow D, Farnan L, Hendrix L, Giovinazzo H, Song G, Gehrig P, Bae-Jump V, Bensen JT, **Zamboni WC**. The effect of body habitus on the innate immune system and pharmacology of carrier-mediated agents and biologics. Interdisciplinary Nutrition Sciences Symposium 2019.

5. Madariaga A, O'Malley DM, Thacker PH, Wenham RM, Mehta A, Bowering V, Cao L, **Zamboni WC**, Nixon A, Bedard P, Wang L, Hassan R, Siu L, Moscow J, Lheureux S. A randomized phase II study of bevacizumab and either weekly anetumab ravtansine or weekly paclitaxel in platinum-resistant or refractory ovarian cancer. Submitted to ASCO TIPS 2019.

6. Juric D, Papadopoulos K, Tolcher A, Do K, Orlando D, **Zamboni W**, Hodgson G, di Tomaso E, Stephens K, Roth D, Shapiro G. Proof-of-Mechanism Based on Target Engagement and Modulation of Gene Expression Following Treatment with SY-1365, a First-in-Class Selective CDK7 Inhibitor in Phase 1 Patients with Advanced Cancer. EORTC-NCI-AACR Conference 2018.

7. Kirschbrown WP, Lucas AT, **Zamboni WC**, Garg A. Biomarkers of Fc-gamma receptors (FcɣRs) on Mononuclear Phagocyte System (MPS) Cells in Blood of Patients with Advanced Gastric Cancer are upregulated as compared to Patients with Metastatic Breast Cancer. EORTC-NCI-AACR Conference 2018.

8. Price LP, Stern S, Kabanov A, **Zamboni WC**. Evaluating the efficiencies and deficiencies of nanoparticle tumor delivery and disposition. Annual Investigators' meeting of the NCI Alliance for Nanotechnology in Cancer 2018.

9. Beaudoin JJ*, Herity LB*, Razo J*, Price LSL*, Sketch MR, Kabanov AV, Lucas AT, **Zamboni WC**. Pharmacokinetic and Allometric Scaling Studies of Nanoparticle Formulations of Anthracyclines. GPEN 2018.

10. Chang SX, Rivera JN, Price LSL*, Herity LB*, Madden AJ*, Roques JR, Santos C, Darr D, **Zamboni WC**. Pharmacokinetic (PK) and pharmacodynamic (PD) studies of PEGylated liposomal doxorubicin (PLD) enhanced delivery to tumors after microbeam radiation therapy (MRT) compared with broadbeam radiaton therapy (BRT) in a triple negative breast cancer mouse model. NCI CCNE PI Meeting 2017.

11. Price LSL*, Stern ST, Kanaby MC*, Eve SG*, Deal AM, Kabanov AV, **Zamboni WC**. Evaluation of nanoparticle drug delivery to tumors: Effects of pharmacokinetic study design and metrics on liposomal delivery to tumors. NCI CCNE PI Meeting 2017.

12. Lucas AT*, Herity LB*, Kornblum ZA, Madden AJ*, Gabizon A, Layko D, Kabanov AV, Ajamie T, Bender DM, Kulanthaivel P, Sanchez-Felix MV, Havel HA, **Zamboni WC**. Use of mononuclear phagocyte platforms to characterize nanomaterials, nanoparticles and colloids. FIP/USP/AAPS Workshop on Nanomedicines – Technical and Regulatory Perspectives 2017.

13. McSweeney MD, Price LSL*, Herity LB*, Wessler T, Cao Y, Forest MG, **Zamboni WC**, Lai SK. The impact of anti-PEG antibodies on the pharmacokinetics and biodistribution of Doxil *in vivo* and *in silico*. Submitted to the Keystone Conference on Immunology.

14. Chang SX, Rivera JN, Herity LB*, Price LSL*, Madden AJ*, Roques JR, Santos C, Darr D, **Zamboni WC**. Comparison of microbeam versus conventional broadbeam radiation therapy on tumor delivery enhancement of PEGylated liposomal doxorubicin in a triple negative breast cancer mouse model. AACR 2017. Cancer Res 2017;77(13 Suppl): Abstract nr 5051. doi:10.1158/1538-7445.AM2017-5051.

15. Salch S*, **Zamboni WC**, Eckel SE. Identifying pharmacy practice patterns and predictors associated with surface contamination of hazardous drugs in pharmacies: a descriptive summary of five commonly used antineoplastic agents. ASHP 2016.

16. Lucas AT*, Herity LB*, Kornblum ZA, Madden AJ*, Gabizon A, Layko D, Kabanov AV, Ajamie T, Bender DM, Kulanthaivel P, Sanchez-Felix MV, Havel HA, **Zamboni WC**. Pharmacokinetic and screening studies of the interaction between mononuclear phagocyte system and nanoparticle formulations and colloid forming drugs. 2016 ACCP Annual Meeting. #41101.

17. Wang H, Markman B, DeSouza P, Kefford R, Dees EC, Gangadhar T, Piha-Paul SA, **Zamboni WC**, Murphy C, Senderowicz A. A dose-escalation study of weekly intravenous CRLX301 in patients with advanced solid tumor malignancies. Submitted to ESMO 2016.

18. Bokhart MT, Schorzman A, Lucas A*, **Zamboni WC**, Muddiman DC. Visualization of small molecule and nanoparticle anticancer agents in tissue and tumor sections using IR-MALDESI mass spectrometry imaging. ASMA 2016.

19. Markman B, DeSouza P, Dees EC, Gangadhar TC, Cooper A, Roohullah A, **Zamboni WC**, Murphy C, Senderowicz, Wang H. A phase 1 study of CRLX301, a novel nanoparticle-drug conjugate (NDC) containing docetaxel (DOC), in patients with refractory solid tumors. ASCO 2016. #2526.

20. Risselada M, Linder KE, Griffith E, Roberts BV*, Davison GS, **Zamboni WC**, Messenger KM. Subcutaneous administration of carboplatin in pluronic F127 in a rodent model. Duke NC State Comparative Oncology Symposium. Feb 2016.

21. Hartman LK, Dhruv HD, Householder KT, Roth JE*, Schorzman AN, **Zamboni W**, Sirianni R, Berens ME. Intravenous delivery of erlotinib-loaded PLA-PEG nanoparticles for glioblastoma. AACR 2016. #1329.

22. **Zamboni WC**, Markman B, de Souza P, Dees EC, Gangadhar TC, Eliasof S, Murphy C, Senderowicz A, Wang H. Pharmacokinetics (PK) of CRLX301, a Novel Nanoparticle-Drug Conjugate (NDC) Containing the Payload Docetaxel, in Patients with Refractory Solid Tumors. AACR 2016, #2047.

23. Salch SA, **Zamboni WC**, Eckel SF. The use of a surface detection kit to identify occupational hazardous drug exposure: identifying pharmacy practice patterns and predictors associated with surface contamination of docetaxel. ASHP 2015.

24. Chang XS, Madden AJ*, Rivera J, Santos C, Darr D, Hunter L, **Zamboni WC**. Use of microbeam radiation therapy to increase the tumor delivery of PEGylated liposomal doxorubicin in a triple negative breast cancer GEM model. Submitted to American Association of Physics in Medicine 2015.

25. Dhruv HD, Hartman LK, Householder KT, Roth JE*, Schorzman AN, **Zamboni WC**, Sirianni R, Berens ME. Intravenous delivery of erlotinib-loaded PLA-PEG nanoparticles for treatment of glioblastoma. Submitted to SNO-SCIDOT Joint Conference on Therapeutic Delivery to the CNS 2015.

26. Chang XS, Madden AJ*, Rivera J, Santos C, Darr D, Hunter L, **Zamboni WC**. The effects of microbeam radiation therapy on the tumor pharmacokinetics of PEGylated liposomal doxorubicin in a triple negative breast cancer GEM model. Submitted to AACR 2015.

27. Bori F*, Madden A*, Kumar P*, Moore S*, Ramanathan R, **Zamboni WC**. Effect of Obesity and Hormones on Pharmacokinetics and Pharmacodynamics of PEGylated Liposomal CKD-602 (S-CKD602). Presented at the Annual Biomedical Research Conference for Minority Students 2013.

28. Eckel SF, McAdoo WF*, Sherwood CA*, O'Neal SK, **Zamboni WC**. Evaluation of Hazardous Drug Clean (HDClean), a two-step towelette system, in removing surface contamination of hazardous drugs. Presented at FIP Annual Meeting 2013.

29. Karginova O, Adamo B, Deal A, Santos C, Darr D, Bash R, Sandison K*, **Zamboni W**, Miller R, Anders C. Efficacy of Carboplatin alone or with ABT888 in a BRCA-mutated, basal-like, Triple Negative Breast Cancer (TNBC) intracranial murine model. Presented at SABCS 2013.

30. Schorzman AN, Chu K, Finniss M, Bowerman C, Kuijer J, Madden A, DeSimone J, **Zamboni W**. An LC-MS/MS Assay for Simultaneous Quantitation of Docetaxel and its Prodrug-Conjugate for Pharmacokinetic Studies of PRINT-Lipidized-Docetaxel Nanoparticles in Mice. Proceedings ASMS 2013, #1203.

31. Madden A*, Rawal S*, Chu K, Sandison K*, Schell R*, Feng L, Ma P, Mumper R, DeSimone J, **Zamboni WC**. Meta-analysis evaluating the efficiency of tumor and tissue delivery of carrier-mediated agents (CMA) and small molecules (SM) using a novel pharmacokinetic (PK) metric relative distribution index over time (RDI-OT). 2013 Proceedings of AACR, #3366.

32. Song G*, Darr DB, Santos CM, Kim M, Midkiff BR, Feinberg NN, Miller CR, Rogers A, Dudley AC, Perou CM, **Zamboni WC**. Relationship between Tumor Microenvironment, Tumor Delivery, and Efficacy of PEGylated Liposomal Doxorubicin (PLD) and Non-liposomal doxorubicin (NL-doxo) in Genetically Engineered Mouse Models (GEMMs) of Breast Cancer (BC). 2013 Proceedings of AACR, #3365.

33. Caron W*, Song G*, Kumar P*, Lay J, Gehrig P, **Zamboni W**. Phenotypically profiling the factors affecting the pharmacokinetics and pharmacodynamics of nanoparticles in preclinical models and in patients. Society of Toxicology Annual Meeting, San Antonio, TX, March 2013.

34. Hinkal G, Hull L, Mazar A, **Zamboni W**. The Animal Models Working Group: Index and Best Practices. NCI Alliance for Nanotechnology in Cancer; Annual Principal Investigator Meeting. November 2012.

35. Caron WP*, Song G*, Lay JC, Madden AJ*, Schorzman A, O'Neal S, Gehrig PA, Decuzzi P, **Zamboni WC**. PhenoGLO-HTSP: A High Throughput Screening Platform that Profiles the Bi-Directional Interaction between Nanoparticle Agents and the Mononuclear Phagocyte System (MPS). NCI Alliance for Nanotechnology in Cancer; Annual Principal Investigator Meeting. November 2012.

36. Caron WP*, Lay JC, Santos C, Merricks EP, Nichols TC, Ramanathan RK, Gehrig PA, **Zamboni WC**. Relationship between interspecies variability in the mononuclear phagocyte system and nanoparticle pharmacokinetics. 2012 Proceedings of 24th EORTC-NCI-AACR Symposium on 'Molecular Targets and Cancer Therapeutics, #59.

37. Song G*, Moore SM*, Tarrant TK, Dobrovolskaia MA, Barrow DA, Kumar P*, Newman SE, Bae-Jump V, Gehrig PA, **Zamboni WC**. Relationship between complement factors and CC chemokines and the pharmacokinetics (PK) and pharmacodynamics (PD) of PEGylated liposomal doxorubicin (PLD) in patients with refractory epithelial ovarian cancer (EOC). 2012 Proceedings of 24th EORTC-NCI-AACR Symposium on 'Molecular Targets and Cancer Therapeutics, #126.

38. Giovinazzo H*, Kumar P*, Sheikh A, Ivanovic M, Walsh M*, Caron WP*, Song G*, Whitlow A, Newman S, La-Beck N*, Kowalsky R, Zamboni B, Clarke-Pearson D, Brewster W, Van Le L, Bae-Jump V, Gehrig P, **Zamboni W**. Technetium-99m Sulfur Colloid (TSC) as a phenotypic probe for predicting

pharmacokinetics (PK) and palmar-plantar erythrodysesthesia (PPE) toxicity of PEGylated liposomal doxorubicin (PLD) in patients with recurrent epithelial ovarian cancer (EOC). October 22, 2012. ACCP 2012 Annual Meetin, #27991.

39. Benhabbour SR, Peng L, Feng L, Ma P, Luft JC, Kim D, **Zamboni WC**, Liu R, Dees C, Haroon Z, DeSimone J, Mumper RJ. Development and evaluation of lipid-based nanocapsules of taxane conjugates versus standard-of-care treatment in an orthotopic non-small cell lung cancer xenograft model. CCNE Annual Meeting 2012.

40. Napier M, Chu K, Finniss M, Schorzman A, Rawal S, Luft C, Bridges A, Boweman C, **Zamboni WC**, DeSimone JM. Pharmacokinetics and efficacy of PLGA PRINT docetaxel and acid-sensitive lipidized docetaxel prodrug in xenograft and orthotopic models. CCNE Annual Meeting 2012.

41. Chu K, Hasan W, Walsh M*, Finniss M, Schorzman A, Rawal S*, Luft C, Bridges A, Bowerman C, Napier ME, **Zamboni WC**, DeSimone JM. Pharmacokinetics of PRINT formulations of docetaxel and an acid-sensitive docetaxel prodrug in xenograft mouse models. C-CCNE Site Visit 2012.

42. **Zamboni WC**, Caron WP, Song G, Kumar P, Rawal S, Newman S, Schorzman A, Barrow D, Tarrant T, Van Le L, Brewster W, Clarke-Pearson D, Bae-Jump V, Gehrig P. Phenotypic Probing of the Interaction between PEGylated Liposomal Doxorubicin (Doxil) and the Mononuclear Phagocyte System as a Method to Individualize Therapy in Patients with Refractory Ovarian Cancer. Submitted to Ovarian Cancer: Prevention, Detection and Treatment of the Disease and Its Recurrence - Molecular Mechanisms and Personalized Medicine 2012.

43. Hugh Giovinazzo*, Kumar P*, Walsh MD*, Caron WP*, Song G*, Sheikh A, Ivanovic M, Whitlow AB, Newman S, La-Beck NM*, Kowalsky RJ, Zamboni BA, Pearson-Clarke DL, Brewster WR, Van Le L, Bae-Jump V, Gehrig PA. **Zamboni WC**. Technetium-99m sulfur colloid (TSC) as a phenotypic probe for predicting Pharmacokinetics (PK) and Palmar-Plantar Erythrodysesthesia (PPE) toxicity of PEGylated liposomal doxorubicin (PLD) in patients (pts) with recurrent epithelial ovarian cancer (EOC). Proceedings of ASCO 2012, #5050.

44. Caron WP*, Lay JC, Kumar P*, Fong AM, La-Beck NM*, Newman SE, Pearson-Clarke DL, Brewster WR, Van Le L, Bae-Jump V, Gehrig PA. **Zamboni WC**. Cellular function of the mononuclear phagocyte system (MPS) as a phenotypic probe for pharmacokinetics (PK) and pharmacodynamics (PD) of PEGylated liposomal doxorubicin (PLD) in patients with recurrent ovarian cancer. Proceedings of ASCO 2012, #2591.

45. La-Beck NM*, Walko CM, Scoggins L*, Dees EC, Orlowski RZ, Wu H*, Amantea M, Fardin M, **Zamboni WC**. Evaluating the effects of bortezomib (Velcade) on the pharmacokinetics of pegylated liposomal doxorubicin (Doxil, PLD). Proceedings of AACR 2012, #3768.

46. Kumar P*, Caron WP*, Song G*, Gallagher K, Clarke-Pearson DL, Brewster WR, Van Le L, Bae-Jump V, Gehrig PA, **Zamboni WC**. Relationship between serum hormone levels and pharmacokinetics (PK) of PEGylated liposomal doxorubicin (PLD) in patients with refractory ovarian cancer. Proceedings of AACR 2012, #2673.

47. Song G*, Tarrant TK, Barrow DA, Gehrig P, Hull JH, Hanna SK, Strychor S, Ramalingam S, Belani CP, Edwards RP, Ramanathan RK, **Zamboni WC**. The effect of CC chemokine ligand-2 (CCL2/MCP-1) and CC chemokine ligand-5 (CCL5/RANTES) on the pharmacokinetics (PK) and pharmacodynamics (PD) of PEGylated liposomal CKD-602 (S-CKD602) in patients with advanced solid tumors. Proceedings of AACR 2012, #754.

48. Ko EM, Lippman Q, Caron WP*, Zamboni B, **Zamboni WC**, Gehrig PA. Palmar-Plantar Erythrodysesthesia (PPE) in patients with liposomal doxorubicin: Can we predict who may be at increased risk? Submitted to SGO 2012.

49. Leed MGD, Pacyniak E, Sadgrove MP, Kagel JR, Armour RC, **Zamboni WC**, Jay M. Biodistribution and pharmacokinetic analysis of a multi-ester prodrug following administration to rats. Proceedings of AAPS 2011, #W4417.

50. **Zamboni WC**, Caron WP*, Song G*, Kumar P*, Rawal S*, Walsh M*, Newman S, Hanna S, Schorzman A, Barrow D, Tarrant T, Van Le L, Brewster W, Clarke-Pearson D, Bae-Jump V, Gehrig P. Phenotypic probing of the bi-directional interaction between PEGylated liposomal agents and the mononuclear phagocyte system in patients and preclinical models. ILS Liposome Advances Conference 2011.

51. Anders CK, Adamo B, Walsh MD*, Karginova O, Darr D, Deal AM, Santos C, Bash R, Hanna SK, Carey, LA, Miller CR, Sharpless N, Perou CM, **Zamboni WC**. Pharmacokinetic disposition of PEGylated liposomal doxorubicin compared with non-liposomal doxorubicin in an intracranial breast cancer murine model. San Antonio Breast Cancer Symposium (SABCS) 2011.

52. Ko EM, Lippman Q, Caron WP*, Zamboni WC, Gehrig PA. Clinical Risk Factors of Doxil Induced Palmar-Plantar Erythrodysesthesia in Recurrent Ovarian Cancer Patients. MAGOS 2011.

53. Wade K, Hanna S, Blackledge J, McGhee W, Fitch R, **Zamboni W**. Method development to minimize ex vivo generation of cisplatin-DNA adducts in tumors. AAPS 2011.

54. Tarantino LM, Ervin RB, Duan H, Cook S, **Zamboni WC** Chung W, Zou F and Wiltshire T. A mouse inbred strain survey of cocaine locomotor activation and pharmacokinetics. International Behavioural and Neural Genetics Meeting, Rome, Italy, 2011.

55. La-Beck NM, Reedy M, Vega J, Weidanz JA, Leff R, Rawat A, Meek C, **Zamboni WC**, Ybarra G, Fardin M, Markiewski M. Complement components as immune biomarkers for predicting toxicities and response to anticancer nanoparticles. Gordon Research Conf on Cancer Nanotechnology 2011.

56. Walsh MD*, Giovinazzo H*, Sheikh A, Ivanovic M, Whitlow AB, Newman S, La-Beck NM*, Kowalsky RJ, Zamboni BA, Clarke-Pearson DL, Brewster WR, Van Le L, Bae-Jump V, Gehrig PA, **Zamboni WC**. Technetium-99m sulfur colloid (TSC) as a phenotypic probe for the pharmacokinetics (PK) and pharmacodynamics (PD) of PEGylated liposomal doxorubicin (PLD) in patients (pts) with recurrent epithelial ovarian cancer (EOC). Proceedings of ASCO 2011, #2582.

57. Caron WP*, Lay JC, Fong AM, La-Beck NM*, Newman SE, Clarke-Pearson DL, Brewster WR, Van Le L, Bae-Jump V, Gehrig PA, **Zamboni WC**. Cellular function of the mononuclear phagocyte system (MPS) as a phenotypic probe for pegylated liposomal doxorubicin (PLD) pharmacokinetics (PK) in patients with recurrent ovarian cancer. Proceedings of ASCO 2011, #2550.

58. Sidone BJ*, Zamboni BA, **Zamboni WC**. Meta-analysis of the pharmacokinetic variability of liposomal anticancer agents compared with non-liposomal anticancer agents. Proceedings of ASCO 2011, #2583.

59. Wu H*, Ramanathan RK*, Zamboni BA, Strychor S, Ramalingham S, Edwards RP, Friedland DM, Stoller RG, Belani CP, Maruca LJ*, Bang YJ, **Zamboni WC**. Mechanism-based pharmacokinetic-pharmacodynamic model characterizing the bi-directional interaction between PEGylated liposomal CKD-602 (S-CKD602) and monocytes in patients with advance malignancies. Proceedings of AAPS-NBC 2011, #87.

60. Schell RF*, Caron WP*, Walsh MD*, Zamboni BA, Ramanathan RK, **Zamboni WC**. Relationship between pharmacokinetic sampling schema and reported PK variability of liposomes in patients. Proceedings of AACR 2011, #1295.

61. Morgan KP*, Caron WP*, Walsh MD*, Zamboni BA, **Zamboni WC**. Comparison of toxicity and study design issues of nanoparticle and small molecule anticancer agents in preclinical models and phase I clinical trials. Proceedings of AACR 2011, #371.

62. Caron WP*, Clewell H, Dedrick R, Ramanathan RK, Yu N, Schellens JH, Beijnen JH, **Zamboni WC**. Allometric scaling of the pharmacokinetics of pegylated liposomal anticancer agents. Proceedings of AACR 2011, #373.

63. Tarantino LM, Ervin RB, Duan H, Cook S, **Zamboni WC** and Wiltshire T. A mouse inbred strain survey of cocaine locomotor activation and pharmacokinetics. Mouse Genetics 2011, Washington, DC, 2011.

64. Caron WP*, Wu H*, Gehrig PA, Song G*, Walsh MD*, Hanna SK, Newman SE, Gabizon A, Ramanathan R, **Zamboni WC**. Factors affecting the pharmacokinetic and pharmacodynamic disposition of nanosomal anticancer agents in patients. Proceedings of AACR Special Conference on Nano in Cancer 2011, #B25.

65. Tarantino LM, Ervin RB, Duan H, Cook S, **Zamboni WC**, Chung W, Zou F and Wiltshire T. Genome-wide association mapping in inbred mice identifies loci involved in cocaine-induced locomotor activation. The Genetics and Epigenetics of Substance Abuse: NIDA/NIAAA Satellite Symposium at the World Congress of Psychiatric Genetics, Washington, DC, 2011.

66. Eckel SF, Hoang V*, Schell R*, Hanna SK, Boswell-Vilt E, **Zamboni WC**. Detecting environmental contamination from the use of docetaxel and paclitaxel in various hospitals in the United States. ASHP 2010.

67. Caron CP*, Wu H*, La-Beck NM*, Song G*, Walsh MD*, Hanna SK, Gabizon A, Ramanathan R, **Zamboni WC**. Factors affecting the pharmacokinetics (PK) and pharmacodynamics (PD) of nanoparticle and nanosomal anticancer agents. Accepted to the EORTC-AACR-NCI Meeting 2010.

68. Caron CP*, Clewell H, Dedrick R, Ramanathan R, Yu N, Tonda M, Schellens JH, Beijen JH, **Zamboni WC**. Preclinical and translational pharmacology of nanoparticle therapeutics. Accepted to American College of Toxicology Meeting 2010.

69. Adamo B, Darr DB, Usary JE, Harrell JC, Meng H, Kafri T, Deal AM, **Zamboni WC**, Miller CR, Anders CK. Preclinical development of an intracranial triple negative breast cancer (TNBC) brain metastasis model: a pilot study. Submitted to ESMO Meeting 2010.

70. Mi Z, Burns V, **Zamboni WC**, Kuo P. Preclinical development of osteopontin aptamer as adjuvant therapy for metastatic breast cancer. RNA Therapeutics Meeting 2010.

71. La-Beck NM*, Wu H*, Infante JR, Jones SF, Burris HA, Keedy V, Kodaira H, Ikeda S, Ramanathan RK, **Zamboni WC**. The evaluation of gender on the pharmacokinetics (PK) of pegylated liposomal anticancer agents. Proceedings of ASCO 2010, #13003.

72. Combest AJ, Zorn KK, Edwards RP, Hanna SK, Habibi S. Strange M, Zamboni BA, Krivak TC, Sukumvanich P, **Zamboni WC**. Pharmacokinetic (PK) of oxaliplatin (OX) after intraperitoneal (IP) and intravenous (IV) administration in patients with gynecological malignancies. Proceedings of ASCO 2010, #2584.

73. Armour RC, Borts DJ, Juliano RL, Fisher MH, Huang L, **Zamboni WC**. An LC-Orbitrap mass spectrometry assay for quantitative bioanalysis of therapeutic small interfering RNA (siRNA). ASMS Conference 2010, #1880.

74. Walsh MD*, La-Beck NM*, Caron WP*, Song G*, Hanna SK, Newman S, Cook S, Bridges A, Walko CW, Armour R, Borts D, **Zamboni WC**. Pharmacologic methods for the translational development of nanoparticle and carrier-mediated agents. NC Nanotech Commercialization Meeting 2010.

75. Walsh MD*, Hanna SK, Sen JM*, Benson JD, Cabral CB, Yurkovetskiy A, Lowinger TB, Zamboni BA, **Zamboni WC**. Pharmacokinetics (PK) of XMT-1001, a novel polymeric prodrug of camptothecin, in mice bearing HT-29 human colon carcinoma xenografts. Proceedings of AACR 2010, #3696.

76. Combest AJ*, Roberts PJ, Dillon PJ, Habibi S, Eiseman JL, Strychor Hanna SK, Muller M, Brunner M, Ross CM, Sharpless NE, **Zamboni WC**. Plasma and tumor pharmacokinetics (PK) of carboplatin in genetically engineered mouse models of melanoma (GEMMs), murine melanoma, and in patients with cutaneous melanoma. Proceedings of AACR 2010, #4203.

77. Caron WP*, La-Beck NM*, Fong AM, Liu P, Hanna SK, Zamboni BA, Gehrig PA, Tarrant T, **Zamboni WC**. Evaluation of monocyte and granulocyte function with and without *ex vivo* pegylated liposomal doxorubicin (PLD) exposure in blood of healthy volunteers. Proceedings of AACR 2010, #3697.

78. Song G*, Wu H*, La-Beck NM*, Zamboni BA, Strychor S, Santory MM, Deitcher SR, **Zamboni WC**. Effect of gender on pharmacokinetic disposition of pegylated liposomal CKD-602 (S-CKD602) and Optisomal topotecan (TLI) in rats, Proceedings of AACR 2010, #3700.

79. Hoang V*, Eckel S, Tu HC*, Hanna SK, Boswell-Vilt E, **Zamboni WC**. Results on the detection of contaminants from the use of docetaxel and paclitaxel chemotherapy in the work environment via ChemoGLO™. Proceedings of HOPA 2010, #T12.

80. Wu H*, La-Beck NM*, Gehrig P, Song G*, Caron W*, Walsh MD*, Hanna SK, Gabizon A, Ramanathan R, **Zamboni WC**. Factors affecting the pharmacokinetics and pharmacodynamics of pegylated liposomal anticancer agents. International Liposome Society Meeting 2009.

81. Wu H*, Infante JR, Jones SF, Burris HA, Chan E, Keedy VL, Bendel JC, Zamboni BA, Kodaira H, Ikeda S, **Zamboni WC**. Factors affecting the pharmacokinetics (PK) and pharmacodynamics (PD) of pegylated liposomal irinotecan (IHL-305) in patients with advanced solid tumors. Proceedings of AACR-NCI-EORTC 2009, #C127.

82. Hoang V*, Eckel S, Tu HC*, Hanna SK, **Zamboni WC**. Detection of contaminants from the use of docetaxel and paclitaxel chemotherapy in the work environment via ChemoGLO™. Proceedings of ASHP 2009, #183011.

83. La-Beck NM*, Gehrig P, Sheikh A, Fong A, Tarrant T, Walsh MD*, Caron W*, Song G*, Ivanovic M, Bai X, Hanna SK, **Zamboni WC**. Pharmacologic methods and phenotypic probes for the translational development of nanoparticle agents. Proceedings of 4th NCI Alliance for Nanotechnology in Cancer Meeting 2009, #15.

84. Roberts PJ, Combest AJ*, Dillion P, Muller M, Brunner, Hanna SK, Sharpless N, **Zamboni WC**. Genetically engineered mouse model of melanoma recapitulates carboplatin tumor disposition in melanoma patients. Proceedings of International Melanoma Congress 2009, #326.

85. Odunsi K, Ghamande SA, Yu AYC*, Lele S, Macfee M, Rodabaugh K, Thomas B, **Zamboni WC**. A Phase II, pharmacokinetic (PK) and pharmacodynamic (PD) study of weekly docetaxel (DOC) in patients with platinum resistant ovarian cancer. Proceedings of ASCO 2009: #3880.

86. Wu H*, Ramanathan RK, Strychor S, Zamboni BA, Ramalingam S, Edwards RP, Friedland DM, Stoller RG, Belani CP, **Zamboni WC**. Population pharmaokinetic of PEGylated liposomal CKD-602 (S-CKD602) in patients with advanced solid tumors. Proceedings of ASCO 2009: #2545.

87. Jones SF, **Zamboni WC**, Burris HA, Chan E, Infante JR, Wu H*, Keedy V, Bendell JC, Lee W, Ikeda S, Rothenberg M. Phase I and pharmacokinetic (PK) study of IHL-305 (PEGylated Liposomal Irinotecan) in patients with advanced solid tumors. Proceedings of ASCO 2009: #2547.

88. La-Beck NM*, Zamboni BA, Tzemach D, Schmeeda H, Sapir R, Gabizon A, **Zamboni WC**. Evaluation of the Relationship between Patient Factors and the Reduction in Clearance of Pegylated Liposomal Doxorubicin. Proceedings of ASCO 2009: #2548.

89. La-Beck NM*, Gehrig PA, Shiekh A, Hanna SK, Tarrant T, Van Le L, Fong A, Ivanovic M, Kowakski, R, Lee C, Bae-Jump V, Qaqish B, **Zamboni WC**. Phenotypic measures of the reticuloendothelial system as predictors of Doxil pharmacokinetics and pharmacodynamics in patients with recurrent gynecologic malignancies. Presented at the C-CCNE NCI Site Visit, May 2009.

90. Benquet C, Lessard D, Le Garrec D, Kujawa P, Palusova D, Courtemanche L, Bichat F, Raguin O, Bari V, Taga S, Smith DC, **Zamboni WC**. DDS-06E – A novel oral pH-sensitive micellar formulation of SN-38: Antitumor efficacy in colon and pancreatic xenograft models. Proceedings of AACR 2009: #1704.

91. **Zamboni WC**, Schorzman DA, Kindig JP, La-Beck NM*, Di J, Hubby B, Kaimal V, Weiser WE. Tumor and tissue disposition of folic-acid-targeted and non-targeted PRINT nanoparticles of polyethylene glycol (PEG) and gadolinium in mice bearing NCI-H125 human lung adenosquamonas carcinoma xenografts. Proceedings of AACR 2009: #3670.

92. La NIM*, Gehrig PA, Sheikh A, LaLush DS, Huang L, Jay M, DeSimone J, Hanna SK, Bridges A, Wu H*, Napier M, Walko CM, Borts D, **Zamboni WC**. The development of nanosomal and nanoparticle anticancer agents: pharmacologic methods and phenotypic probes for pharmacokinetic (PK) and pharmacodynamic (PD) disposition. Carolina Center of Cancer Nanotechnology Excellence (CCCNE) Annual Meeting 2009, #312

93. **Zamboni WC**, Marshall JL, Strychor S, Sidone BJ*, Zamboni BA, Malik S, Hansen N, Catley K*, Grafton K*, Hwang JJ. Pharmacokinetic (PK) and pharmacodynamic (PD) study of the combination of docetaxel (Doc) and Oxaliplatin (Oxal) in patients with advanced solid tumors. Proceedings of ASCO 2008: #2546.

94. Lessard D, Gori S, Palusova D, Courtemanche L, Le Garrec D, Benquet C, Baille W, Kujawa P, Smith D, Taga S, **Zamboni WC**. Antitumor response and pharmacokinetic studies of an orally administered pH-sensitive micellar formulation of SN38 using a polymeric nanodelivery system (SN38-PNDS) in preclinical models. Proceedings of AACR 2008 #510.

95. **Zamboni WC**, Strychor S, Sidone BJ*, Santory M, Berryman D, Moran H, Deitcher SR, Abutin RM. Pharmacokinetic study of Optisomal topotecan (topotecan liposomal injection, TLI, OPTISOME) and non-liposomal topotecan in male Sprague-Dawley rats. Proceedings of AACR-NCI-EORTC 2007: #C113.

96. Sidone BJ*, Edwards RP, Zamboni BA, Strychor S, Maruca LJ*, **Zamboni WC**. Evaluation of body surface area (BSA) based dosing, age, and body composition as factors affecting the pharmacokinetic (PK) variability of STEALTH liposomal doxorubicin (Doxil). Proceedings of AACR-NCI-EORTC 2007: #C107.

97. Tolcher AW, Batist G, Sarantopoulos J, Fontanilla J, Lu B, Moran T, **Zamboni WC** Choy GS, Deitcher SR. A phase I and pharmacokinetic study of Alocrest (vinorelbine liposomes injection, OPTISOME) in patients with advanced solid tumors, non-Hodgkin's lymphoma, and Hodgkin's disease. Proceedings of AACR-NCI-EORTC 2007: #100.

98. Chen Y, Pandya K, Smudzin T, Strychor S, Sidone BJ*, **Zamboni WC**. Phase II and pharmacokinetic (PK) study of induction docetaxel and cisplatin with RHG-CSF and concurrent pulsed docetaxel chemoradiation for stage III non-small cell lung cancer. Accepted to the 12th World Conference on Lung Cancer 2007.

99. **Zamboni WC**, Edwards RP, Mountz JM, Eiseman JL, Basse PH, Zamboni BA, DeLoia JA, Donnelly MK*, Rohan LC, Ramanathan RK, Strychor S. The Development of Liposomal and Nanoparticle Anticancer Agents: Methods to Evaluate the Encapsulated and Released Drug in Plasma and Tumor and Phenotypic Probes for Pharmacokinetic (PK) and Pharmacodynamic (PD) Disposition. Proceedings of NSTI Nanotechnology Conf 2007: #1582.

100. Wonganan P, **Zamboni WC**, Strychor S, Dekker JD, Roessler B, Sidone Croyle MA. Drug-Virus Interaction: Effect of Administration of Recombinant Adenovirus on the Pharmacokinetics of Docetaxel in Rats. American Society of Gene Therapy in Feb'07.

101. Chen Y, Pandya K, Smudzin T, Strychor S, Sidone B*, **Zamboni WC**. Phase II and pharmacokinetic (PK) study of induction docetaxel and cisplatin with RHG-CSF and concurrent pulsed docetaxel chemoradiation for stage III non-small cell lung cancer (NSCLC). Proceedings of ASCO 2007: #18142.

102. Maruca LJ*, Ramanathan RK, Strychor S, Zamboni BA, Ramalingam S, Edwards RP, Kim JK, Bang YJ, Lee HY, **Zamboni WC**. Age-related effects on the pharmacodynamic (PD) relationship between STEALTH liposomal CKD-602 (S-CKD602) and monocytes in patients with refractory solid tumors. Proceedings of ASCO 2007: #2576.

103. **Zamboni WC**, Maruca LJ*, Strychor S, Zamboni BA, Ramalingam S, Edwards RP, Friedland DM, Stoller RG, Ramanathan RK. Age and body composition related-effects on the pharmacokinetic disposition of STEALH liposomal CKD-602 (S-CKD602) in patients with advanced solid tumors. Proceedings of ASCO 2007: #2528.

104. Florian JA, Egorin MJ, **Zamboni WC**, Eiseman JL, Lagattuta TF, Belani CP, Chatta GS, Scher HI, Solit DB, Parker RS. A physiologically based pharmacokinetic (PBPK) and pharmacodynamic model (PD) of docetaxel and neutropenia in humans. Proceedings of ASCO 2007: #2567.

105. **Zamboni WC**, Strychor S, Joseph E, Zamboni BA, Parise RA, Yu YY, Engber C, Eiseman JL. Fat and skeletal muscle disposition of STEALTH liposomal CKD-602 (S-CKD602) and non-liposomal CKD-602, a camptothecin analogue, in SCID mice. Proceedings of AACR 2007: #1470.

106. Strychor S, Eiseman JL, Parise RA, Joseph E, Egorin MJ, **Zamboni WC**. Fat and skeletal muscle disposition of docetaxel in SCID mice. Proceedings of AACR 2007: #1529.

107. Odunsi K, Ghamande S, Andrews C, Strychor S, DeLoia J, Thomas B, Rodabaugh K, Macfee M, Lele S, **Zamboni WC**. Pharmacokinetic study of weekly docetaxel (DOC) in patients with platinum resistant ovarian cancer. Accepted to Society of Gynecological Oncology 2007.

108. **Zamboni WC**, Friedland DM, Ramalingam S, Edwards RP, Stoller RG, Belani CP, Strychor S, Ou YC, Tonda ME, Ramanathan RK. Final results of a phase I and pharmacokinetic study of STEALTH liposomal CKD-602 (S-CKD602) in patients with advanced solid tumors. Proceedings of ASCO 2006, 24;82s: #2013.

109. Florian JA, **Zamboni WC**, Eiseman JE, Strychor S, Joseph E, Parise RA, Egorin MJ, Parker R. Physiologically based modeling of docetaxel in mice bearing SKOV3 human ovarian xenografts. Proceedings of AACR 2006; #360.

110. Strychor S, Eiseman JE, Joseph E, Parise RA, Tonda ME, Yu NY, Engber C, **Zamboni WC**. Plasma, tissue, and tumor disposition of STEALTH liposomal CKD-602 (S-CKD602) and non-liposomal CKD-602, a camptothecin analogue, in mice bearing A375 human melanoma xenografts. Proceedings of AACR 2006, 47;721: #3064

111. **Zamboni WC**, Eiseman JE, Strychor S, Rice PM, Joseph E, Potter DM, Shurer J*, Walsh DR*, Parise RA, Tonda ME, Yu NY, Engber C, Basse PH. Relationship between the plasma and tumor disposition of STEALTH liposomal CKD-602 and macrophages/dendritic cells (MDC) in mice bearing human tumor xenografts. Proceedings of AACR 2006, 47;1280: #5449.

112. **Zamboni WC**, Strychor S, Joseph E, Walsh DR*, Parise RA, Tonda ME, Yu NY, Engber C, Eiseman JE. Plasma and tumor disposition of STEALTH Liposomal CKD-602 (S-CKD602) and non-liposomal CKD-602, a camptothecin analogue, in mice bearing A375 human melanoma xenograft. Proceedings of AACR-NCI-EORTC 2005: #B173.

113. Hwang JJ, Malik S, Moore DJ, McGrievy J, Park S, **Zamboni WC**, Marshall JL. A phase I and pharmacokinetic study (PK) of docetaxel (DOC) and oxaliplatin (OX). Proceedings of ASCO 2005: #2105.

114. Creaven PJ, **Zamboni WC**, Ramnath N, Javle MM, Strychor S, Repinski TVW, Zamboni BA, Schwartz JK, French RA, Fakih MG. A phase I and pharmacokinetic (PK) study of weekly docetaxel (D), cisplatin (P), and daily capecitabine (C) in patients with advanced solid tumors. Proceedings of ASCO 2005: #2047.

115. **Zamboni WC**, Belani CP, Ramalingam S, Friedland DM, Stoller RG, Modi NB, Nath RP, Tonda ME, Strychor S, Ramanathan RK. Phase I and pharmacokinetic study of STEALTH liposomal CKD-602 (S-CKD602) in patients with advanced solid tumors. Proceedings of ASCO 2005: #2069.

116. Strychor S, Eiseman JL, Parise RA, Egorin MJ, Joseph E, **Zamboni WC**. Plasma, tumor, and tissue disposition of docetaxel in SCID mice bearing SKOV-3 human ovarian xenografts. Proceedings of AACR 2005: #4165.

117. **Zamboni WC**, Whitner H, Potter DM, Ramanathan RK, Strychor S, Tonda ME, Stewart BE, Modi NB, Engber C, Dedrick RL. Allometric Scaling of STEALTH liposomal anticancer agents. Proceeding of AACR 2005: #1394.

118. Chatta GS, Fakih M, Ramalingam R, Belani CP, Ramanathan RK, Zamboni W, Friedland D, Lis D, Tutchko S, Egorin M. Phase I and pharmacokinetic study of daily imatinib in combination with docetaxel for patients with advanced solid tumors. Proceedings of ASCO 2004: #2047.

119. Goel S, Mani S, Iqbal T, Desai K, Parise RA, Afroze R, Egorin MJ, **Zamboni WC**. The effect of food on the oral absorption of 9-nitrocampothecin (9NC) in patients with relapsed solid tumors. Proceedings of ASCO 2004: #2106.

120. Fakih MG, **Zamboni WC**, Ramanath N, Javie MM, Schwarz JK, French RE, Regal LL, Ramanathan RK, Gorenflo RK, Creaven PJ. A phase I and pharmacokinetic (PK) study of weekly docetaxel (D), cisplatin (P), and daily capecitabine (C) (DPC) in patients with advanced solid tumors. Proceedings of ASCO 2004: #2092.

121. Parise RA, Egorin MJ, Mani S, Jayabalan D, **Zamboni WC**. A novel, liquid chromatography-tandom mass spectrometry (LC-MS/MS) assay for 9-nitrocamptothecin and its 9-aminocamptothecin metabolite in human plasma. Proceedings of AACR 2004: #5410.

122. Eiseman JL, Parise RA, Joseph E, Strychor S, Parker RS, Egorin MJ, **Zamboni WC**. Pharmacokinetics of 9-nitrocamptothecin (9NC) and 9-aminocamptothecin (9AC) in SCID mice bearing human colon xenografts, HT29. Proceeding of AACR 2004: #5401.

123. **Zamboni WC**, Eiseman JL, Muller M, Brunner M, Joseph E, Strychor S, Egorin MJ, Jung LL*. Tumor disposition of carboplatin in mice bearing murine B16 melanoma is not indicative of the disposition of patients with cutaneous melanoma. Proceedings of AACR-Japanese Cancer Assoc 2004: #B21.

124. Stewart C, Chintagumpala M, Ashley D, Kellie S, Iacono L, **Zamboni WC**, Fouladi M, Houghton P, Heideman R, Gajjar A. Results of a phase II upfront window of pharmacokinetically guided topotecan (TPT) in high-risk medulloblastoma (MB) and supratentorial primitive neuroectodermal tumor (SPNET). Proceedings of ASCO 2003: #3234.

125. Chatta G, Fakih M, Friedland D, Ramanathan R, Belani C, Ramalingam S, Stoller R, **Zamboni WC**, Tutchko S, Egorin M. Phase I and pharmacokinetic (PK) study of daily gleevec (STI571) in combination with every three weeks intravenous (i.v.) docetaxel (D) in patients with advanced solid tumors. Proceedings of ASCO 2003: #577.

126. **Zamboni WC**, Belani CP, Jung LL, Egorin ME, Parise RA, Jacobs SA, Shin D, Fakih M, Tutchko S, Ramanathan RK. Phase I and pharmacokinetic study of weekly docetaxel (D) in combination with capecitabine (C) in patients with advanced solid tumors. Proceedings of ASCO 2003: #555.

127. Bulgaru A, Goel S, **Zamboni WC**, Hochster H, Wadler S, Lagattuta T, Freda T, Brisar C, Egorin M, Mani S. Phase I study of oxaliplatin in combination with 5-FU and gemcitabine in patients with solid tumor. Proceedings of AACR: #5348.

128. **Zamboni WC**, Jung L*, Strychor S, Joseph E, Burke T, Curran D, Egorin M, Eiseman J. Plasma and tissue disposition of DB-67 non-liposomal (NL) and bilayer liposomal (BL) in SCID mice. Proceedings of AACR 2003: #1792.

129. Basu S, Goel S, **Zamboni WC**, Wadler S, Hochster H, Sparano J, Rajdev L, Hamilton A, Walko C*, Zuhowski E, Zimmerman M, Jhawer M, Mani S. Phase I and pharmacokinetic study of oxaliplatin in combination with gemcitabine and continuous infusion (CIV) of 5-fluorouracil in patients with advanced solid malignancies. Proceedings of ASCO 2002: #2131.

130. **Zamboni WC**, Jung LL*, Egorin MJ, Jin R, Wong MK, Fakih M, Belani CP, Potter DM, Walko CW*, Tauch JS, Strychor S, Sun SL, Trump DL, Ramanathan RK. Phase I studies of intermittently administered 9-nitrocamptothecin (9NC): relationship between daily dose and toxicity. Proceedings of ASCO 2002: #390.

131. **Zamboni WC**, Jung LL, Hamburger DR, Jin R, Joseph E, Strychor S, Sun SL, Egorin MJ, Eiseman JL. Plasma and tissue disposition of 9-nitrocamptothecin (9NC, rubitecan, RFS2000) and its 9-aminocamptothecin metabolite in mice bearing HT29 human colon xenografts. Proceedings of AACR 2002: #1229.

132. **Zamboni WC**, Hamburger DR, Jung LL*, Jin R, Joseph E, Strychor S, Sun SL, Ramanathan RK, Egorin MJ, Eiseman JL. Relationship Between Systemic Exposure of 9-nitrocamptothecin (9NC, Rubitecan, RFS2000) & its 9-aminocamptothecin (9AC) Metabolite & Response in Human Colon Cancer Xenografts. AACR-NCI-EOTRC Meeting 2001: #400.

133. Gilbert BE, Newman RA, **Zamboni WC**, Knight V, Verschraegen CF. Pharmacokinetics of multiple 9-nitrocamptothecin (9NC) liposome aerosols during a Phase I study: levels of total and lactone forms and its conversion to 9-aminocamptothecin (9AC). Proceeding of ASCO 2001: #536.

134. **Zamboni WC**, Jung LL*, Jin R, Egorin MJ, Wong MKK, Belani CP, Potter DM, Tauch JS, Strychor S, Sun SL, Trump DL, Ramanathan RK. Phase I and pharmacokinetic (PK) study of intermittently administered 9-

nitrocamptothecin (9NC, rubitecan) in patients with advanced malignancies. Proceeding of ASCO 2001: #411.

135. Jung LL*, **Zamboni WC**, Frye RF, Johnson CS, Adedoyin A, Hofacker J, Branch RA, Trump DL. Modulation of All-trans-retinoic acid (ATRA) disposition with ketoconazole and disulfiram in patients with hormone-refractory prostate cancer. Proceeding of ASCO 2001: #446.

136. Vozniak JM*, Stewart CF, Jin R, Coons JC*, Hanna S, Ramanathan RK, Sun SL, Egorin MJ, **Zamboni WC**. Lactone stability of camptothecin analogs in urine: implications for the development of cystitis. Proceedings of AACR 2001: #5021.

137. **Zamboni WC**, Jin R, Delauter BJ*, Egorin MJ, Belani C, Wong M, Tauch JS, Strychor S, Potter DM, Lenaz L, Sun SL, Trump DL, Ramanathan RK. Plasma and urine disposition of 9-nitrocamptothecin (9NC, Rubitecan) & its 9-aminocamptothecin (9AC) metabolite as part of Phase I study of intermittently administered rubitecan. Proceedings of 11th NCI-EORTC-AACR Symposium on New Drugs in Cancer Therapy, November 2000: #242.

138. **Zamboni WC**, Gervais AC*, Schellen JHM, Delauter BJ*, Egorin MJ, Zuhowski EG, Pluim D, Hamburger DR, Working PK, Colbern G, Eiseman JL. Disposition of platinum (Pt) in B16 murine melanoma tumors after administration of cisplatin & pegylated liposomal-cisplatin formulations (SPI-077 & SPI-077 B103). Proceedings of 11th NCI-EORTC-AACR Symposium on New Drugs in Cancer Therapy, November 2000: #132.

139. **Zamboni WC**, Gervais AC, Egorin MJ, Schellens JHM, Delauter BJ, Zuhowski EG, Pluim D, Hamburger DR, Eiseman JL. Inter- and Intratumoral Disposition of Platinum (Pt) in B16 Murine Melanoma Tumors after Administration of Cisplatin. Proceeding of ACCP 2000: #325.

140. Working P, Slater J, Colbern G, Schellens J, **Zamboni WC**, Huang A. Encapsulation of cytotoxic drugs in STEALTH liposomes: relationship of pharmacokinetics, toxicity, and activity. Presented at the Fourth International Liposome Conference.

141. Tkaczuk KH, Hussain A, Tait N, DeSchields M, Hamden H, Rehner J, Quinn C, **Zamboni WC**, Hausner PF. A Phase I study of doxorubicin (DOX), docetaxel (DOC), and gemcitabine (GEM) combination (TAG) in patients (pts) with solid tumors. Proceedings of American Society of Clinical Oncology, 2000: #852.

142. Stewart CF, Lui CY, **Zamboni WC**, Ma MM, Kirstein MN, Hanna SK, Gajjar AJ, Santana VM, Houghton PJ, Sambol NC. Population pharmacokinetics of topotecan in children and adolescents. Proceedings of American Society of Clinical Oncology, 2000: #687.

143. Delauter BJ*, Ramanathan RK, Stover LL, Zuhowski EG, Egorin MJ, Plunkett WK, **Zamboni WC**. Pharmacokinetics of gemcitabine and 2'-2'-difluorodeoxyuridine in a patient with ascites. Proceedings of American Society of Clinical Oncology, 2000: #921C.

144. **Zamboni WC**, Jin R, Vaughn MT, Zuhowski EG, Egorin MJ. High performance liquid chromatography (HPLC) assay with methanolic extraction for 9-nitrocamptothecin (9NC, RFS2000) and 9-aminocamptothecin (9AC). Proceedings of the American Association for Cancer Research, 2000: #3425.

145. Ma MK, Gajjar AJ, Ashley DM, Kellie SJ, Strother D, Kun LE, **Zamboni WC**, Danks MK, Stewart CF. Individualized topotecan (TPT) dosing attains cytotoxic CSF TPT exposures in children with high-risk medulloblastoma. Proceedings of the Society of Neuro-oncology 1999.

146. **Zamboni WC**, Egorin M, Doyle A, Nemieboka N, Dobson J, Tait N, Fedenko K, Van Echo D, Tkaczuk K. Pretreatment with topotecan decreases docetaxel clearance and increases toxicity. Proceedings of the American Society of Clinical Oncology 1999: #631.

147. **Zamboni WC**, Egorin MJ, Schellens JHM, Grimm AE*, Kunska AK, Sentz DL, Zuhowski EG, Pluim D, Eiseman JL. Factors affecting platinum exposure and formation of platinum-DNA adducts (Pt-DNA) in B16 murine melanoma tumors after cisplatin (CDDP) administration. Proceedings of the 8th International Symposium on Platinum and Other Metal Coordination Compounds in Cancer Chemotherapy 1999.

148. Luftner D, Possinger D, Schweigert M, Sezer O, Dobson J, Egorin M, **Zamboni WC**. Increasing topotecan (TPT) infusion from 30-minutes to 4-hours infusions prolongs the duration of exposure in the cerebrospinal fluid (CSF). Proceedings of the American Association of Cancer Research 1999: #735.

149. **Zamboni WC**, Egorin M, Grimm A, Stewart J, Sentz D, Zuhowski E, Eiseman D. Disposition of unbound- and total-platinum in B16 murine melanoma tumors after cisplatin administration. Proceedings of the American Association for Cancer Research 1999: #2596.

150. **Zamboni WC**, D'Argenio, D, Stewart CF, MacVittie T, Tubergen D, Egorin MJ. Pharmacodynamic model of topotecan induced time-course of neutropenia. Proceedings of the American Association for Cancer Research1999: #736.

151. **Zamboni WC**, Egorin MJ, Dobson JM, Zuhowski EG, Farese AM, MacVittie T. Pharmacokinetics (PK) of high dose topotecan (TPT) in a nonhuman primate model. Proceedings of the American College of Clinical Pharmacy, Cincinnati 1998.

152. McCune J, Lindley C, Socinski MA, Donahue A, **Zamboni WC**, Stewart C. Targeting topotecan (TPT) systemic exposure in combination with carboplatin (CAR) and etoposide (ETOP) in small cell lung cancer (SCLC). Proceedings of the American Society of Clinical Oncology 1998.

153. Stewart CF, Ma M, Furman WL, Santana VM, **Zamboni WC**, Gajjar A, Houghton PJ. Pharmacokinetics of Irinotecan and its active metabolite SN-38 in children with recurrent solid tumors after protracted low dose intravenous administration. Proceedings of American Society of Clinical Oncology 1998.

154. Thompson J, **Zamboni WC**, Stewart CF, Houghton PJ. Therapeutic synergy of topotecan in combination with vincristine for treatment of xenografts representing several childhood malignancies. Proceedings of AACR 1998: #527.

155. Gajjar AJ, **Zamboni WC**, Houghton PJ, Danks MK, Heideman RL, Reardon D, Thompson S, Kun L, Stewart CF. Rationale for pharmacokinetically targeted Phase II trial of topotecan (TPT) in newly diagnosed patients with medulloblastoma/PNET. Proceedings of The American Society of Pediatric Hematology Oncology 1997.

156. Houghton PJ, Stewart CF, **Zamboni WC**, Thompson J, Santana VM. Rational design of clinical trials in children with camptothecin analogs based upon optimization of efficacy in xenograft models. Proceedings of the European Cancer Society 1997.

157. **Zamboni WC**, Houghton PJ, Mandrell T, Einhause S, Rogers W, Gajjar A, Heideman R, Stewart CF. Topotecan cerebrospinal fluid disposition (CSF) disposition in the nonhuman primate model: implications for topotecan use in children with medulloblastoma. Proceedings of the American College of Clinical Pharmacy 1997.

158. Santana VM, **Zamboni WC**, Houghton P, Stewart CF. Use of preclinical models and pharmacokinetics to define new schedules and dosing strategies of topotecan in pediatric malignancies. Proceedings of The American Society of Pediatric Hematology Oncology 1997.

159. Stewart CF, Gajjar AJ, Heideman RL, Houghton PJ, **Zamboni WC**. Phenytoin increases topotecan (TPT) clearance in a patient with medulloblastoma (MB). Proceedings of the American Society of Clinical Oncology 1997: #1012.

160. Santana V, **Zamboni WC**, Gajjar A, Pappo A, Houghton P, Meyer W, Stewart C. Pharmacokinetically guided use of topotecan (TPT) given (daily x 5) x2, in children with solid tumors. Proceedings of ASCO 1997: #511.

161. **Zamboni WC**, Santana V, Gajjar AJ, Meyer WH, Pappo A, Houghton PJ, Stewart CF. Pharmacokinetically guided dose adjustment reduces variability in topotecan (TPT) systemic exposure in children with solid tumors. Proceedings of ASCO1997: #205.

162. **Zamboni WC**, Houghton P, Hulstein J, Crom W, Thompson J, Cheshire P, Stewart C. Relationship between tumor extracellular fluid (ECF) exposure and tumor response in human neuroblastoma xenografts. Proceedings of the American Association for Cancer Research 1997.

163. **Zamboni WC**, Houghton PJ, Hulstein J, Thompson JC, Cheshire PJ, Stewart CF. Probenecid inhibits systemic and renal clearance of topotecan. Proceedings of the American Society for Clinical Pharmacology and Therapeutics 1997. Clin Pharmcol Therap 1997; 61:145.

164. **Zamboni WC**, Stewart CF, Thompson J, Houghton PJ. The relationship between systemic exposure to topotecan and tumor response in human neuroblastoma xenografts. Proceedings of the Seventh Conference on DNA Topoisomerases in Therapy 1996.

165. Stewart CF, **Zamboni WC**, Gajjar A, Kun L, Heideman R. Clinical pharmacokinetics of topotecan in plasma and CSF, experimental and clinical data. Proceedings of the Second Congress of the European Association for Neuro-Oncology, Wurzburg, Germany. J Neuro-Oncol 1996; 30:163.

166. **Zamboni WC**, Crom WR, Houghton PJ, Thompson JC, Stewart CF. Plasma protein binding of SN-38, the active metabolite of irinotecan. Proceedings of the Annual Meeting of American College of Clinical Pharmacy, Nashville, TN, August 1996. Pharmacother 1996; 16:500.

167. Bowman LC, Stewart CF, **Zamboni WC**, Crom WC, Luo X, Heideman R, Houghton PJ, Meyer WH, Pratt CB. Toxicity and pharmacodynamics of oral topotecan (POTOPO) in pediatrics patients with relapsed solid tumors. Proceedings of ASCO 1996: #462.

168. **Zamboni WC**, Heideman RL, Meyer WH, Gajjar AJ, Crom WR, Stewart CF. Pharmacokinetics (PK) of topotecan (TPT) in pediatric patients with normal and altered renal function. Proceedings of ASCO 1996; #371.

169. Stewart CF, **Zamboni WC**, Crom WR, Houghton PJ, Pratt CB. Pharmacokinetics of DMP-840 in children with relapsed solid tumors. Proceedings of AACR 1996: #181.

170. **Zamboni WC**, Crom WR, Bowman LC, Pratt CB, Houghton PJ, Stewart CF. Interpatient variability in oral (PO) absorption of topotecan (TPT) in children with relapsed solid tumors. Clin Pharmacol Ther 1996; 59:198.

171. Piscitelli SC, **Zamboni WC**, Wells M, Metcalf J, Baseler M, Stevens R, Lane C and Kovacs J. Co-modeling of interleukin-2 as a function of soluble IL-2 receptors in HIV-infected patients. Pharmacotherapy 1995; 15:389.

Submitted:

1. Harvey RD, Selvaggi G, Ross J, Zhou J, Chen Z, Chen L*, **Zamboni W**, Dees EC, MD5A phase 1 trial of MRX-2843, a novel dual MerTK inhibitor, in patients with advanced or metastatic solid tumors. Submitted to ASCO'24.

INVITED TALKS

1. The Effect of Body Habitus on Precision Dosing of Complex Drugs and Biologics. The University of Texas College of Pharmacy Rho Chi Ceremony. April 2023.

2. Effect of Viral Infections on Innate Immune System and Pharmacology of Complex Drugs. ASPET Webinar Sept 2023.

3. Pharmacologic Studies of the Mononuclear Phagocyte System as Part of Clinical Studies of Anetumab Ravtansine: Interim Analysis. Anetumab Ravtansine Clinical Team, UM1 ETCTN, CTEP, NCI. Feb 2022.

4. Minibeam Radiation Therapy Enhanced Delivery of Nanoparticle Anticancer Agents to Pancreatic Cancer Tumors. NCI Alliance for Nanotechnology in Cancer Program Meeting. Oct 2021.

5. Effect of Body Habitus and Race on the Innate Immune System and the Pharmacology of Complex Drugs and Biologics. UNC TREND, UNC LCCC. Oct 2021.

6. Translational Studies of the Innate Immune System as Biomarkers for the Pharmacology of Complex Drugs and Biologics: A Model for Team Pharmaceutical Sciences. WVU School of Pharmacy. Nov 2018.

7. Biomarkers of the Mononuclear Phagocytic System (MPS) for the Pharmacokinetics and Pharmacodynamics of the Antibodies and Antibody Drug Conjugates. PEGS Summit: Clinical Progress in Antibody-Drug Conjugates. Boston, MA. May 2018.
8. Evaluating the Efficiencies and Deficiencies of Nanoparticle Tumor Delivery and Disposition, CCNE Site Visit to UNC. Chapel Hill, NC. February 2018.
9. Relationship between the Mononuclear Phagocyte System and the Pharmacokinetics and Pharmacodynamics of Antibody Drug Conjugates in Patients. PEGS Boston – Antibody-Drug Conjugates. Boston, MA. May 2017.
10. Pharmacokinetics and Pharmacodynamics of Nanoparticles; Bi-directional Interaction between Nanoparticle Agents and the Mononuclear Phagocyte System. The Carolina Nanoformulations Workshop, Chapel Hill, NC. 2017.
11. Evaluation of the Bi-Directional Interaction between the Mononuclear Phagocyte System (MPS) and the Pharmacokinetics and Pharmacodynamics of Carrier Mediated Agents and Antibody-Drug Conjugates. PEGS Boston – Antibody Drug Conjugates II: Advancing Towards the Clinic. Boston, MA. April 2016.
12. Factors affecting the clearance, distribution, and tumor delivery of carrier-mediated agents. Barrow Neurological Institute. Phoenix, AZ. Feb 2016.
13. Understanding the factors affecting the PK of nano agents in preclinical models and in patients as a method to improve the therapeutic index. Applied Pharmaceutical Nanotechnology (APN) meeting. Cambridge, MA. Nov 2015.
14. Bi-directional interaction between mononuclear phagocyte system and nanoparticles in blood, tumor and tissues. American Society of Nanomedicine. Crystal City, VA. Oct 2015.
15. Interactions between tumor microenvironmental factors and nanomedicines which influence tumor delivery and efficacy. American Society of Nanomedicine. Crystal City, VA. Oct 2015.
16. Bi-directional interaction between the mononuclear phagocyte system and liposomal agents in preclinical models and patients. 24th Annual Southeast Lipid Research Conference. Stone Mountain, GA. Sept 2015.
17. Preclinical Characterization of ADME, PK, PD, and toxicology of Nanoformulations; Use of nano agents in non-cancer diseases; Factors affecting nano delivery to tumors in animal models and patients; Clinical PK and PD (efficacy and toxicity) aspects of nano agents. Carolina Nanoformulations Workshop, UNC Eshelman School of Pharmacy. 2015.
18. Interactions between the mononuclear phagocyte system, carrier-mediated agents and antibody drug conjugates. Americas Antibody Congress 2015. San Diego, CA. May 2015.
19. Translational studies evaluating the bi-directional interaction between the mononuclear phagocyte system and carrier-mediated agents. National Center for Toxicological Research. Jefferson, AK. May 2015.
20. Bi-directional interaction between the mononuclear phagocyte system and nanoparticle pharmacokinetics and pharmacodynamics in preclinical models and patients. University of Kentucky, Lexington, KY. May 2015.
21. Bi-directional interaction between the mononuclear phagocyte system and nanoparticle pharmacokinetics and pharmacodynamics: Influence on Accelerated Blood Clearance. Moderna Symposium on Accelerated Blood Clearance of Nanoparticles. Boston, MA. March 2015.
22. Translational Studies Evaluating the Bi-directional Interaction between Carrier-Mediated Anticancer Agents and the Mononuclear Phagocyte System. 36th EORTC-PAMM Winter Meeting, Marseille Provence Metropole, France. January 2015.
23. Workshop: Profiling the Factors that Alter the Tumor Delivery of Carrier-Mediated Agents. World ADC Conference, San Diego, CA. Nov 2014.

24. Factors Affecting the Pharmacokinetics and Pharmacodynamics of Nanparticles, Carrier-Mediated Agents and Antibody Drug Conjugates: Similarities and Connections. World ADC Conference, San Diego, CA. Nov 2014.

25. Pharmacokinetics and Pharmacodynamics of Nanoparticles and Carrier-Mediated Agents in Preclinical Animal Models and in Patients. CACO-PBSS Cancer Nanotherapeutics Workshop, San Francisco, CA. April 2014.

26. NIH/NIAID/DAIDS Workshop on Long Acting / Extended-Release Antiretroviral Drugs, Boston, MA, March 2014.

27. Safety and ADMET Aspects of Nanotechnology in Parenteral Drug Products. US FDA and PQRI Workshop on Nanomaterial Drug Products: Current Experience and Management of Potential Risks, Silver Spring, MD, Jan 2014.

28. Profiling the Interaction between Nanoparticle and Carrier-Mediated Agents and the Mononuclear Phagocyte System in Blood, Tumors and Tissues. CT3N Symposium, University of Pennsylvania, Nov 2013.

29. Profiling the Factors affecting Nanoparticle and Carrier-Mediated Agent Clearance and Delivery to Tumors and Tissues. PKUK Meeting, Harrogate, North Yorkshire, UK, Oct 2013.

30. Evaluation of Factors Affecting Nanoparticle Pharmacokinetics and Pharmacodynamics in Preclinical Models and Patients: A focus on Patient Characteristics and the Mononuclear Phagocyte System. Pharmacoepidemiology Seminar Series, UNC School of Medicine, Chapel Hill, NC, Oct 2013.

31. Profiling the Factors affecting Nanoparticle Clearance and Delivery to Tumors and Tissues. Department of Pharmacology, Harvard University, Boston, MA, Oct 2013.

32. Novel Methods, Models and Pharmacologic Results to Guide the Translational Development of Nanoparticle and Carrier-Mediated Agent. Department of Pharmacology, UNC School of Medicine, Oct 2013.

33. Novel pharmacologic and phenotypic methods to characterize carrier-mediated and nanoparticle agents as part of preclinical and clinical development. 2nd International Conference and Exhibition on Biowaivers and Biosimilars, Raleigh, NC, Sept 2013.

34. Phenotypically profiling the factors affecting the pharmacokinetics and pharmacodynamics of nanoparticle agents in preclinical models and in patients. Society of Toxicology Annual Meeting, San Antonio, TX, March 2013.

35. Evaluation of the mononuclear phagocyte system (MPS) and effects on nanoparticle pharmacokinetics and pharmacodynamics in preclinical animal models and in patients. Nanomedicines Alliance Industry Symposium on Nanomedicines: Charting a Road to Commercialization. Rockville, MD, March 2013.

36. Profiling the biological factors modulating nanoparticle clearance, biodistribution and tumor delivery in preclinical animal models and in patients. NCI Alliance for Nanotechnology in Cancer Annual Principal Investigator Meeting, Biodistribution Working Group Session, Houston, TX, November 2012.

37. Profiling the bi-directional interaction between nanoparticle agents and the mononuclear phagocyte system: effects on clearance and tumor delivery of nanoparticle agents. NIH/NCI TONIC / Alliance for Nanotechnology in Cancer / Industry Workshop on Enhanced Permeability and Retention (EPR) Effect and Nanomedicine Drug Targeting in Cancer, NIH, Bethesda, MD, October 2012.

38. Factors affecting the bi-directional interaction between liposomal agents and the mononuclear phagocyte system. AAPS Webinar, September 2012.

39. Profiling the biological factors modulating drug delivery in preclinical animal models and in patients. Invited speaker for the 2012 Drug Carriers in Medicine and Biology Gordon Research Conference, Waterville Valley Resort, NH, August 2012.

40. Influence of the MPS on the clearance and tumor delivery of nanoparticle agents. In the session on Pharmacokinetics of Nanoparticles – Understanding Interactions at the Nano/Bio Interface, AAPS National Biotechnology Conference, San Diego, CA, May 2012.

41. Phenotypic probing of the mononuclear phagocyte system as a method to individualize therapy with PEGylated liposomal doxorubicin (PLD) in patients with refractory ovarian cancer. Ovarian Cancer: Prevention, Detection and Treatment of the Disease and Its Recurrence – Molecular Mechanisms and Personalized Medicine. University of Pittsburgh Cancer Institute, Pittsburgh, PA, 2012.

42. Technetium-99m sulfur colloid (TSC) as a phenotypic probe for predicting the pharmacokinetics and pharmacodynamics of PEGylated liposomal doxorubicin (PLD; Doxil) in patients with recurrent epithelial ovarian cancer. UNC Nuclear Medicine Division of Radiology Meeting, May 2012.

43. Pharmacologic methods and resources to facilitate the translational development of carrier-mediated and nanoparticle agents. Northwestern University Center for Cancer Nanotechnology Excellence, Chicago, IL, April 2012.

44. Factors affecting the pharmacokinetics and pharmacodynamics of nanoparticle agents in preclinical models and in patients. ASME Early-Stage Research Collaboration Nano Engineering for Medicine and Biology Workshop, Washington DC, April 2012.

45. PhenoGLO: Novel platforms to profile nanoparticle agents and individualize nanoparticle therapy. Nanotechnology Commercialization Conference, Durham, NC, April 2012.

46. Phenotypic probing of the mononuclear phagocyte system as a method to individualize PEGylated liposomal doxorubicin (Doxil) therapy in patients with refractory ovarian cancer: Results of UNC LCCC clinical study. UNC LCCC Gynecologic Oncology Group, Chapel Hill, NC, March 2012.

47. Overview of nanoparticle anticancer agents and pharmacologic issues. UNC LCCC Phase I Program Seminar, Chapel Hill, NC, March 2012.

48. Age related effects on the pharmacokinetics and pharmacodynamics of PEGylated-liposomal anticancer agents: Alterations in MPS function? UNC LCCC Geriatric Oncology Program, Chapel Hill, NC, February 2012.

49. Phenotypic probing of the bi-directional interaction between PEGylated liposomal agents and the mononuclear phagocyte system. Carolina Center of Cancer Nanotechnology Excellence Seminar, Chapel Hill, NC, February 2012.

50. Unique pharmacologic resources to evaluate and improve the preclinical and clinical development of carrier-mediated and nanoparticle agents. Center for Innovation for Nanobiotechnology (COIN) and NanoMedicine Partnering Mission of Medicon Valley of Denmark and Sweden Meeting, Chapel Hill, NC, January 2012.

51. Phenotypic probing of the bi-directional interaction between PEGylated liposomal agents and the mononuclear phagocyte system. International Liposome Society Liposome Advances Conference, London, England, December, December 2011.

52. Novel pharmacokinetic and pharmacodynamic metrics to profile the systemic, tumor and tissue disposition of nanoparticle agents. Nanoparticle Biodistribution: Physical and Biological Effects at the NCI Alliance for Nanotechnology in in Cancer Investigators' Meeting, Boston, MA, September 2011.

53. Pharmacologic and animal model pitfalls for the translational development of nanoparticle agents as part of the symposium on Nanotechnology in Products: Pitfalls and Successes in the Path to a Commercial Product at the MANCEF/COMS Nanotechnology Meeting, August 2011. Panel Member.

54. Lessons learned in the translation from animals to humans for pharmacokinetics and pharmacodynamics of nanoparticle agents. Nanomedicine Product Development Summit: Turning Nanoparticle Delivery Systems into Innovative Medicines. Controlled Release Society Meeting, July 2011. Panel Member.

55. Factors affecting the pharmacokinetics and pharmacodynamics of nanoparticle agents in animal models and in patients. Pharmacologic and Regulatory Issues for the Translational Development of Nanoparticle Agents Workshop, Controlled Release Society Meeting, July 2011, Co-Chair.

56. Pharmacologic methods to improve the translational development of nanoparticle agents. Department of Pharmacology, East Carolina University, May 2011.

57. Factors Affecting the Translational Development of Nanoparticle Agents. Department of Pharmacology, Wake Forest University, April 2011.

58. Mechanistic PK-PD Modeling of the Bi-directional Interaction between PEGylated Liposomal Anticancer Agents and Monocytes. AAPS National Biotechnology Conference, April 2011.

59. How to improve the translational development of nanoparticle agents via pharmacologic methods. NC Society of Toxicology Meeting, March 2011.

60. Factors affecting the pharmacokinetics (PK) and pharmacodynamics (PD) of nanoparticle and nanosomal anticancer agents. EORTC-AACR-NCI Meeting, November 2010.

61. Preclinical and translational pharmacology of nanoparticle therapeutics. American College of Toxicology Meeting, October 2010.

62. Bi-Directional Pharmacokinetic and Pharmacodynamic Interaction between PEGylated Liposomal Anticancer Agents and the Reticuloendothelial System. International Liposome Research Days, August 2010.

63. Pharmacology and Toxicology Issues Affecting the Translational Development of Nanoparticle Agents. NCI Best Practices in Cancer Nanotechnology Workshop, June 2010.

64. Evidence and Clinical Practice Experience of Pharmacokinetic Monitoring of 5-FU for Colorectal Cancer. HOPA Annual Meeting, March 2010.

65. Age Related Effects on the Pharmacokinetic and Pharmacodynamics of Liposomal and Nanoparticle Anticancer Agents. UNC LCCC Geriatric Oncology Program. March 2010.

66. Factors Affecting the Pharmacokinetics and Pharmacodynamics of Liposomal and Nanoparticle Agents. AAPS Webinar, February 2010.

67. Factors Affecting the Pharmacokinetics and Pharmacodynamics of PEGylated Liposomal Anticancer Agents. International Liposome Society Liposome Advances Conference, London, England, December 2009.

68. Factors Affecting the Pharmacology of PEGylated Liposomal Agents in Patients. Fourth Annual NCI Alliance for Nanotechnology in Cancer Investigators Meeting, October 2009.

69. Individualizing Pegylated Liposomal Doxorubicin (PLD) Treatment in Patients with Ovarian Cancer. UNC LCCC Board of Visitors Meeting. August 2009.

70. Factors Affecting the Pharmacokinetics and Pharmacodynamics of Nanosomal Anticancer Agents: Evaluation of the Reticuloendothelial System, Chapel Hill Drug Conference, University of North Carolina, Chapel Hill, NC in May 2009.

71. Development of Phenotypic Probes of the Reticuloendothelial System as Part of the Translational Development of Nanosomal and Nanoparticle Anticancer Agents, UNC Institute for Pharmacogenetics and Individualized Therapy Seminar Series, Feb 2009.

72. Evaluation of the Reticuloendothelial System as Part of the Translational Development of Nanosomal Anticancer Agents, UNC Pathology and Laboratory Medicine Grand Rounds, February 2009.

73. Translational Development of Nanosomal and Nanoparticle Anticancer Agents, UNC Gynecology Oncology Grand Rounds, January 2009.

74. Influence of the Reticuloendothelial System on the Pharmacokinetics and Pharmacodynamics of Nanosomal and Nanoparticle Anticancer Agents, Philadelphia College of Pharmacy and Sciences, Pharmaceutical Sciences Dept, Grand Rounds, January 2009.

75. Factors Affecting the Pharmacokinetics and Pharmacodynamics of Nanosomal Anticancer Agents: Evaluation of the Reticuloendothelial System. Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics in April 2008.

76. Evaluation of the Reticuloendothelial System as Part of the Preclinical and Clinical Development of Liposomal and Nanoparticle Anticancer Agents. Moffitt Cancer Center, Tampa FL in Nov'06; Nanoparticle Characterization Laboratory, National Cancer Institute, Fredrick, MD in Feb 2007.

77. Liposomal and Nanoparticle Anticancer Agents: Magic Bullets N'at. University of Pittsburgh Alumni Association Metro PITT Club Meeting, Pittsburgh, PA, May 2006.

78. Preclinical and Clinical Development of Liposomal Anticancer Agents. FDA, Feb 2006.

79. Novel Methods for Pharmacokinetic Sampling: Use of Microdialysis to Evaluate the Pharmacokinetics and Pharmacodynamics of Drugs. HOPA Annual Meeting, San Diego, CA, June 2005.

80. Optimizing Erythropoietic Growth Factor Formulary Management: 2005 Interchange Opportunities. University Pharmacotherapy Associates Program. January 2005 to Present.

81. Optimizing Outcomes in Chemotherapy-Induced Neutropenia: Synchronized CSF Innovation. University Pharmacotherapy Associates Program. July 2004 to January 2005.

82. Systemic, Tissue, and Tumor Disposition of Stealth Liposomes. University of Pittsburgh School of Pharmacy Alumni Weekend. Seven Springs, PA. June 2002 and Children's Hospital of Philadelphia, March 2004.

83. Use of Microdialysis in Pharmacodynamic Studies of Anticancer Agents. 4th International Symposium on the Pharmacodynamics of Anticancer Agents. Sea Island, GA. September 2001.

84. Use of PET Imaging in the Development of Anticancer Agents. Significant Papers in Pharmacotherapy. The Annual Meeting of the American College of Clinical Pharmacy, Los Angeles, CA. November 2000.

85. Pharmacokinetic Principles and Modeling, Regional Chemotherapy and Tumor Disposition of Anticancer Agents. The Seventh Annual Berlex Oncology Clinical Pharmacology of Anti-Cancer Drugs Course, Leesburg, VA. November 2000.

86. Tumor Disposition of Platinum after Administration of Cisplatin and Liposomal-Cisplatin in Mice Bearing B16 Murine Melanoma Tumors. Fourth Annual Invitational Oncology Pharmacy Conference. St. Thomas, Virgin Islands.

87. Plant Alkaloids. University of Pittsburgh Cancer Institute Comprehensive Chemotherapy Course. Pittsburgh, PA. October 1999.

88. Pharmacokinetic Principles and Modeling, Regional Chemotherapy and Tumor Disposition of Anticancer Agents. The Seventh Annual Berlex Oncology Clinical Pharmacology of Anti-Cancer Drugs Course, Leesburg, VA. October 1999.

89. Factors Affecting Platinum Exposure and Formation of Platinum-DNA Adducts in Solid Tumors. St. Jude Children's Research Hospital, Memphis, TN, May 1999.

90. Factors Affecting Platinum Exposure and Formation of Platinum-DNA Adducts in B16 Murine Melanoma Tumors after Cisplatin Administration. Third Annual Invitational Oncology Pharmacy Research Conference. Napa Valley, CA. February 1999.

91. Pharmacokinetic Principles and Modeling, and Tumor Disposition of Anticancer Agents. The Sixth Annual Berlex Oncology Clinical Pharmacology of Anti-Cancer Drugs Course, Leesburg, VA. October 1998.

92. Use of Microdialysis Methodology to Evaluate Anticancer Agent Disposition in Tumor Extracellular Fluid. Second Annual Invitational Oncology Pharmacy Research Conference. Newport Beach, CA. February 1998.

93. Pharmacokinetically Guided Dose Adjustment Reduces Variability in Topotecan Systemic Exposure in Children with Solid Tumors. St. Jude Children's Research Hospital Postdoctoral Retreat. Memphis, TN. April 1997.

94. Cerebrospinal Fluid Disposition of Topoisomerase I Inhibitors in the Nonhuman Primate Model. St. Jude Children's Research Hospital Postdoctoral Retreat. Memphis, TN. April 1996.

95. Pharmacokinetic and Pharmacodynamic Research of Chemotherapeutic Agents. University of Pittsburgh School of Pharmacy, Pittsburgh, PA. October 1995.

96. Clinical Applications of Gene Therapy to Genetic and HIV Diseases. First Annual Pharmacotherapy Frontiers Symposium. Warren G. Magnuson Clinical Center, National Institutes of Health, Bethesda, MD. May 1995.

97. Evaluation of Ondansetron and Granisetron Cross-Sensitivity and Systemic Exposure Responses. Eastern States Residency Conference. Baltimore, MD. April 1995.

GRANTS

Current Grants:

Source of Support:	Wake Forest University Health Sciences / NIH PAR-20-284 (IPF#23-1748)
Principal Investigators:	Gmeiner, William
Co-Investigator:	Zamboni, William (Consortium PI)
Total Direct Funding:	$701,249
Total Period Support:	07/01/2023 – 06/30/2028
Percent Effort:	5% Effort/ 5% Salary
Project Title:	Nanodelivery of FP polymers to improve treatment of metastatic colorectal cancer

Source of Support:	Deep Creek Pharma, LLC. / NIH PA-22-178 (IPF#23-0461)
Principal Investigators:	Gmeiner, William
Co-Investigator:	Zamboni, William (Consortium PI)
Total Direct Funding:	$416,636 Total UNC Subaward
Total Period Support:	05/01/2023 – 04/30/2025
Percent Effort:	10% Effort/ 10% Salary
Project Title:	STTR: Phase II: Improved Treatment of Colorectal Cancer with CF10

Source of Support:	TransChromix LLC. / NIH PA-22-179 (IPF#23-0755)
Principal Investigators:	Chen, Xian (UNC School of Medicine)
Co-Investigator:	Zamboni, William
Total Direct Funding:	$180,000 (Total UNC Subaward)
Total Period Support:	09/01/2023 – 08/31/2024

Percent Effort:	2% Effort/ 2% Salary
Project Title:	STTR: Novel therapeutic intervention of early-stage T1D

Source of Support:	US FDA_RFA-FD-23-004: Research Triangle Center of Excellence in Regulatory Science and Innovation (CERSI) (U01) Clinical Trials Optional
Principal Investigators:	Watkins, Paul (Contact PI); Halabi, Susan (PI); Samei, Ehsan (PI); and Mentz, Robert J. (PI)
Project PI:	Zamboni, William (Contact Project PI); Bae-Jump, Victoria; Gonzalez, Daniel; and Secord, Angeles A
Total Direct Funding:	Total Costs: $544,250 in Year 1; $544,250 in Year 2
Total Period Support:	09/01/2023 – 08/31/2028 (Total 5-year application)
Percent Effort:	15% effort / 15% salary
Project Title:	Precision Dosing of Immuno-Oncology Antibodies via Biomarkers and/or Metrics associated with the Innate Immune System (IIS) and Body Habitus

Source of Support:	US FDA The Perinatal Health Center of Excellence (PHCE) Grant (NCTR Project # GCDER014)
Principal Investigators:	Wang, Yow-Ming (US FDA PI); Zamboni, William (UNC PI)
Total Direct Funding:	$181,018/year x 2 year
Total Period Support:	01/01/2024 – 12/31/2025
Percent Effort:	18.5% effort / 18.5% support
Project Title:	Evaluating the Effect of Obesity on the Pharmacokinetics and Pharmacodynamics of Monoclonal Antibodies in Pediatric Patients

Source of Support:	NIH - 1R21CA267584-01
Principal Investigators:	V Bae-Jump; W Zamboni
Total Funding:	$427,625
Total Period of Support:	01/31/23 – 12/31/25
Percent Effort:	8% Effort / 8% Salary
Project Title:	Impact of Obesity on Immuno-Oncology Agents in Endometrial Cancer

Source of Support:	NIH 1R01CA247652-01A1
Principal Investigators:	W Zamboni (Lead PI), S. Chang (Co-PI), and S. Libutti (Co-PI)
Total Direct Funding:	$2,792,913 total award of 5 yrs.
Total Period Support:	04/01/21 – 03/31/26
Percent Effort:	23% Effort/ 23% Salary
Project Title:	Minibeam Radiation Therapy Enhanced Delivery of Nanoparticle Anticancer Agents to Pancreatic Cancer Tumors

Source of Support:	NIH - 1R01CA257009-01A1
Principal Investigators:	K. Ainslie
Co-Investigator	W Zamboni
Total Direct Funding:	$1,761,616 Total award; $309,698 to Zamboni's lab of 5 yrs.
Total Period Support:	08/01/21 – 07/31/26
Percent Effort:	4.58% Effort/ 4.58% Salary
Project Title:	Tunable Temporal Drug Release for Optimized Synergistic Combination Therapy of Glioblastoma

Source of Support:	NIH - 1R01CA264488-01
Principal Investigators:	A. Kabanov
Co-Investigator:	W. Zamboni
Total Direct Funding:	$2,452,235 Total award; $182,248 to Zamboni's lab of 4 yrs.
Total Period Support:	08/01/21 – 07/31/25
Percent Effort:	4% Effort/ 4% Salary

Project Title:	Toward Translation of Nanoformulated Paclitaxel-Platinum Combination

Source of Support	NIH / NCI T32 (2-T32-CA196589-06)
Principal Investigators	Kabanov A
Total Period of Support	07/08/2020 – 4/30/2022
Co-Investigator	Zamboni W
Percent Effort	0% Effort / 0% Salary
Project Title	Carolina Cancer Nanotechnology Training Program (C-CNTP)

Source of Support:	NIH/NCI Experimental Therapeutics-Clinical Trials Network with Phase 1 Emphasis (ET-CTN) (UM1) – Biomarker Supplement
Principal Investigators:	W Zamboni
Total Direct Funding:	$100,000
Total Period of Support:	11/01/18 – 12/31/23
Percent Effort:	10% Effort / 10% Salary
Project Title:	Pharmacologic studies of the mononuclear phagocyte system as part of the clinical studies of anetumab ravtansine: Sample Analyses

Source of Support:	NIH - 5UL1TR002489-04
Principal Investigators:	J. Buse
Co-Investigator:	W. Zamboni
Total Direct Funding:	$38,450,854 Total award
Total Period Support:	03/30/18 – 02/28/23
Percent Effort:	5% Effort/ 5% Salary
Project Title:	The North Carolina Translational and Clinical Sciences (TraCS) Institute

Source of Support:	UNC LCCC Development Grant – Tier 2
Principal Investigators:	V Bae-Jump, W Zamboni
Total Direct Funding:	$200,000
Total Period of Support:	12/01/20 – 01/31/24 (NCE)
Percent Effort:	10% Effort / 0% Salary
Project Title:	Atezolizumab and ONC201 as a Novel Treatment Strategy in Obesity-driven Endometrial Cancer

Source of Support:	UNC LCCC Development Grant – Tier 1
Principal Investigators:	W Zamboni, EC Dees
Total Direct Funding:	$49,995
Total Period of Support:	12/01/17 – 06/30/24 (NCE)
Percent Effort:	10% Effort / 0% Salary
Project Title:	Biomarkers of the Mononuclear Phagocytic System as Predictors of the Pharmacokinetics and Pharmacodynamics of the Antibody Drug Conjugate Glembatumumab Vedotin

Current Contracts:

Source of Support:	SciTech Development
Principal Investigator:	W Zamboni
Total Direct Funding:	$138,800
Total Period of Support:	11/01/23 – 10/31/24
Percent Effort of Support:	2% Effort / 2% Salary
Project Title:	Analytical and Pharmacokinetic Studies of Total (Encapsulated + Released) Fenretinide, 4-methoxy- and 5-oxo- Fenretinide Metabolites, and Retinol after administration of Phospholipid Suspension (ST-001) in Plasma from Patients

Source of Support: Inimmune Corporation
Principal Investigator: W Zamboni
Total Direct Funding: $223,741
Total Period of Support: 09/01/23 – 08/31/23
Percent Effort of Support: 5% Effort / 5% Salary
Project Title: Single Dose and Multiple Dose Pharmacokinetic Studies of Total (Encapsulated and Released) INI-4001 for Liposomal INI-4001 and INI-4001 for Non-Liposomal INI-4001 in Plasma, Tumor and Tissues in C57Bl/6 Mice Bearing B16F10 Melanoma Flank Tumors

Source of Support: Xcovery (Task 2)
Principal Investigators: Zamboni W
Total Direct Funding: $254,598 (Total amount is based on number of patients enrolled)
Total Period of Support: 02/01/18 – 02/01/24
Percent Effort: 5% Effort / 5% Salary
Project Title: Analytical and Pharmacokinetic Studies of MRX-2843 and metabolite(s) in Plasma and Urine as part of the Phase 1 Dose Escalation Study of the Safety, Pharmacokinetics and Pharmacodynamics of MRX-2843 in Adult Subjects with Refractory Solid Tumors

Source of Support: ChemoGLO
Principal Investigators: W Zamboni
Total Direct Funding: $12,874/year
Total Period of Support: 09/01/19 – 12/31/24
Percent Effort: 1% Effort / 1% Salary
Project Title: Task 5 - Comparison of Chemotherapy Measurements on Surfaces by LC-MS/MS

Source of Support: ChemoGLO
Principal Investigators: W Zamboni
Total Direct Funding: $48,000/year
Total Period of Support: 01/01/17 – 12/31/25
Percent Effort: 5% Effort / 5% Salary
Project Title: Analysis of Platinum Exposures of Surfaces in Hospitals and Pharmacies

UNC Projects Administered Via the Recharge Center:

Source of Support: Gilead Sciences
Principal Investigators: Mungo, Chemtai
Total Direct Funding: $10,000
Total Period Support: 06/01/2019 – 04/30/2024
Project Title: Pharmacokinetic Analyses of Artesunate Following Intravaginal Administration in Patients in Kenya

Source of Support: University of Alabama Birmingham Medical Center
Principal Investigators: Giri, S
Total Direct Funding: $12,000
Total Period Support: 06/01/2021 – 04/30/2024 (NCE)
Project Title: Optimizing Melphalan dose among older adults with Multiple Myeloma receiving Autologous Stem Cell Transplantation

Source of Support: NIH 1K01TW011191-01_K01 Career Development Award (PSID 5113822)
Principal Investigators: Westmoreland, Kate

Total Direct Funding:	$714,155
Total Period Support:	06/01/2019 – 04/30/2024
Project Title:	Understanding Methotrexate Dosing, Pharmacokinetics, and Toxicities in Patients with Burkitt Lymphoma in Malawi

Source of Support:	NIH R01 DK124617, NIH/NIDDK
Principal Investigators:	Arthur, Janelle Corrinne
Total Direct Funding:	$1,193,579 currently awarded; $1,915,735 (Total award 5-year project)
Total Period Support:	06/01/2020 – 05/31/2025
Project Title:	Microbiota-mediated fibrotic remodeling in the inflamed intestine

Source of Support:	Cincinnati Childrens Hospital Medical Center / FDA (PSID 5126493)
Principal Investigators:	Capal, Jamie Korin
Total Direct Funding:	$50,404
Total Period Support:	09/10/2021 - 06/30/2023
Project Title:	Sirolimus TSC Epilepsy Prevention Study (STEPS)

Research Proposals Pending

Pending Grants:

Source of Support:	State of NC Collaboratory
Principal Investigator:	Yuan, Hong (Lead-PI); Zamboni, William (Co-PI)
Total Direct Funding:	$139,235 (For Zamboni)
Total Period Support:	02/01/2024 – 01/31/2025
Percent Effort:	5% Effort / 5% Salary
Project Title:	Safely enhance CNS cancer drug delivery by spatially fractionated radiation therapy

Source of Support:	American Foundation for Pharmaceutical Education (AFPE)
Principal Investigators:	Clarie O'Connor
Mentor:	Zamboni, William
Total Direct Funding:	$9,600
Total Period Support:	06/01/2024 – 05/31/2025
Percent Effort:	5% Effort/0% Salary
Project Title:	Precision dosing of monoclonal antibodies in obese patients

Source of Support:	fFAME / NIH PA-20-185 (IPF#23-1300) New
Principal Investigators:	Benner, Steven
Co-Investigator:	Zamboni, William (Contact UNC PI), Hingtgen, Shawn (PI) and Dees, Claire (Co-I)
Total Direct Funding:	$ 1,850,308.50
Total Period Support:	04/01/2023 – 03/31/2028
Percent Effort:	10% Effort/ 10% Salary
Project Title:	Synthetic Bio-Medicine Collaboration for Cancer Research, Diagnostics and Therapy

Source of Support:	fFAME Foundation / NCI – RFA-RM-22-020 (IPF#23-0733) New
Principal Investigators:	Benner, Steven E.
Co-Investigator:	Zamboni, William (Contact UNC PI), Hingtgen, Shawn (PI) and Dees, Claire (Co-I)
Total Direct Funding:	$2,110,793
Total Period Support:	08/01/2023 – 07/31/2028
Percent Effort:	15% Effort/ 15% Salary
Project Title:	Creating Synthetic Biology to be Used in the Clinic

Source of Support:	University of Alabama at Birmingham / NIH PAR-21-033 (IPF#23-1034) New
Principal Investigators:	Williams, Grant R.
Co-Investigator:	Zamboni, William
Total Direct Funding:	$446,509
Total Period Support:	07/01/2023 – 06/30/2028
Percent Effort:	15% Effort/ 15% Salary
Project Title:	Preventing Chemotherapy-Induced Neuropathy through Personalized Dosing- the PRECISE Study

Source of Support:	NIH 1R01DK134137-01A1 (IPF#23-0484) Resubmisison
Principal Investigators:	Nguyen, Juliane (Contact PI) and Arthur, Janelle (PI)
Co-Investigator:	Zamboni, William and Sheikh, Shehzad
Total Direct Funding:	$3,834,120
Total Period Support:	04/01/2023 – 03/31/2028
Percent Effort:	8% Effort/ 8% Salary
Project Title:	Engineering Probiotic Yeast for Targeted Treatment of Ulcerative Colitis

Source of Support:	Oregon Health and Science University / NCI – R01 PA-20-185 (IPF#23-0364)
Principal Investigators:	Brody, Jonathan
Co-Investigator:	Zamboni, William (UNC Consortium PI)
Total Direct Funding:	$118,502 (Total UNC Subaward)
Total Period Support:	04/01/2024 – 03/31/2026
Percent Effort:	5% Effort/ 5% Salary
Project Title:	Overcoming Chemoresistance in Pancreatic Ductal Adenocarcinoma with iRGD-targeted PEG:CF10

Source of Support:	TransChromix LLC. / NIH PA-21-262 (IPF#23-0744) Resubmission
Principal Investigators:	Chen, Xian (UNC School of Medicine)
Co-Investigator:	Zamboni, William
Total Direct Funding:	$303,029 (Total UNC Subaward)
Total Period Support:	04/01/2023 – 03/31/2024
Percent Effort:	5% Effort/ 5% Salary
Project Title:	STTR: Novel brain-penetrant strategies for translation-targeting therapeutics of Alzheimer's disease

Source of Support:	NIH 1R01EB034318-01 (IPF#22-5225)
Principal Investigators:	Lai, Sam
Co-Investigator:	Zamboni, William
Total Direct Funding:	$2,921,795
Total Period Support:	04/01/2023 – 03/31/2027
Percent Effort:	8% Effort/ 8% Salary
Project Title:	Engineering biodegradable PEGs that overcome anti-PEG immunity to restore prolonged circulation and efficacy of PEGylated therapeutics

Source of Support:	Wake Forest University Health Sciences / DoD – W81XWH-22-BCRP-BTA12 (IPF#22-4474)
Principal Investigators:	Lo, Hui-Wen
Co-Investigator:	Zamboni, William (Consortium PI)
Total Direct Funding:	$206,366
Total Period Support:	02/01/2023 – 01/31/2025
Percent Effort:	5% Effort/ 5% Salary
Project Title:	Developing Pharmacological Inhibitors of tGLI1 for Breast Cancer Brain Metastasis

Source of Support:	Deep Creek Pharma, LLC. / NIH PA-21-262 (IPF#22-4006)

Principal Investigators:	Gmeiner, William
Co-Investigator:	Zamboni, William (Consortium PI)
Total Direct Funding:	$46,884 Total UNC Subaward
Total Period Support:	12/01/2023 – 11/30/2024
Percent Effort:	9% Effort/ 9% Salary
Project Title:	STTR Phase I: CF10 Nanoparticle Therapy for Colorectal Liver Metastases

Pending Contracts:

None

Research Proposals - Past Funding

UNC - Past Grants:

Source of Support:	NC Biotechnology Center Innovation Impact Grant (IIG)
Principal Investigators:	W Zamboni
Total Direct Funding:	$150,000
Total Period of Support:	Awarded April 4, 2022
Project Title:	A Triple Quadrupole LC-MS/MS System for Bioanalytical Studies Supporting the Translational Development of Complex and Small Molecule Agents

Source of Support:	NIH R01 - 1R01HL141934-04
Principal Investigators:	S Lai (Lead PI), W Zamboni (Co-PI)
Total Direct Funding:	$2,658,480 Total award
Total Period Support:	05/10/2018 – 05/30/2022 (NCE)
Percent Effort:	10% Effort/ 10% Salary
Project Title:	Overcoming anti-PEG immunity to restore prolonged circulation and efficacy of PEGylated therapeutics.

Source of Support:	NIH - 1R01HL153744-01A1
Principal Investigators:	D. Lawrence
Co-Investigator:	W Zamboni
Total Direct Funding:	$2,705,713 Total award; $247,830 to Zamboni's lab of 3 yrs. from 05/01/2022
Total Period Support:	05/01/21 – 11/30/23
Percent Effort:	5% Effort/ 5% Salary
Project Title:	Design and Application of Photoresponsive Modules in Circulating Erythrocytes

Source of Support:	NCI/NIH 1 1R41CA254834-01A1 / STTR - Deep Creek Pharma
Principal Investigators:	W Gmeiner, W Zamboni
Total Direct Funding:	$45,124 – Direct funding for UNC subaward to Zamboni's lab
Total Period of Support:	08/17/21 – 07/31/22 (NCE)
Percent Effort:	10% Effort / 10% Salary
Project Title:	STTR: Phase I: Advanced pre-clinical development of CF10 to improve treatment of metastatic colorectal cancer

Source of Support:	NCTraCS Funding for COVID-19 Research C192034 Intramural
Principal Investigators:	W Zamboni (Lead-PI), M Heise (Co-PI)
Total Direct Funding:	$50,000
Total Period of Support:	06/01/20 – 07/31/22
Percent Effort:	1% Effort Cost Share
Project Title:	Evaluation of innate immune system (IIS) phenotype on COVID-19 incidence, severity, and treatment outcomes

Source of Support:	Center for Health Innovation – Innovation Pilot Award
Principal Investigator(s):	Rahima Benhabbour
Co-Investigator:	W Zamboni (via the UNC ATPAC Recharge Center)
Total Direct Funding:	$5,599
Total Period of Support:	10/23/20 – Present
Project Title:	Lidocaine assay cross-validation and analysis of PK samples of mice treated with mucoadhesive biodegradable films loaded with lidocaine for vulvar pain management.

Source of Support:	NIH / NCI T32-CA009156-35
Principal Investigators:	J Pagano, B Weissman
Total Period of Support:	01/01/16 – 12/31/21
Co-Investigator:	William C. Zamboni
Percent Effort:	0% Effort / 0% Salary
Project Title:	T32 Training Grant in Cancer Research

Source of Support:	1U54CA198999-01 – CCNE Pilot Grant
Principal Investigators:	Zamboni W (Lead-PI), Lockett M (Co-PI)
Total Direct Funding:	$49,860
Total Period Support:	09/01/19 - 06/30/21
Percent Effort:	5% effort/ 0% salary
Project Title:	Modulation of Tumor Fibroblasts by MRX-2843 to Increase the Tumor Delivery and Efficacy of Nanoparticles in In Vivo and In Vitro 3D Tumor Models.

Source of Support:	NIH/NCI Experimental Therapeutics-Clinical Trials Network with Phase 1 Emphasis (ET-CTN) (UM1) – Biomarker Supplement
Principal Investigators:	W Zamboni
Total Direct Funding:	$99,800
Total Period of Support:	11/01/17 – 05/31/21
Percent Effort:	5% Effort / 5% Salary
Project Title:	Pharmacologic studies of the mononuclear phagocyte system as part of the clinical studies of anetumab ravtansine: Assay development and validation

Source of Support:	Emory University Drug Development Fund
Principal Investigators:	W Zamboni
Total Direct Funding:	$6,036
Total Period of Support:	03/01/19 – 06/30/19
Percent Effort:	0.25% Effort / 0.25% Salary
Project Title:	Quantitation of SN38 in Plasma, Tumor and Liver after Administration of HA-SN38 Nanoparticle in Mice

Source of Support:	NC TraCS Institute: 2KR1091802
Principal Investigators:	Zamboni W; Jarstfer M
Total Direct Funding:	$2,000
Total Period of Support:	01/01/19 – 12/31/19
Percent Effort:	5% Effort / 5% Salary
Project Title:	In vitro selection of non-binding ssDNA oligos with high serum nuclease resistance

Source of Support:	1 R43 CA228938-01 SBIR: Phase I Proposal: CBT Pharmaceuticals
Principal Investigators:	Reddy M, W Zamboni
Total Direct Funding:	$48,500 (for Zamboni)
Total Period of Support:	09/20/18 – 02/28/20
Percent Effort:	5% Effort / 5% Salary

Project Title:	Combination of checkpoint inhibitors UNC: Evaluation of the Interaction between CBT-501 & CBT-502 and the Mononuclear

Source of Support:	NSF ASSIST Pilot Study Year 6 – NC State University
Principal Investigators:	D Carpenter (Co-PI); W Zamboni (Co-PI); Michael Daniele (Co-I)
Total Direct Funding:	$59,936
Total Period of Support:	11/01/17 – 10/31/18
Percent Effort:	10% Effort / 0% Salary
Project Title:	Evaluation of the Pharmacokinetics of Lisinopril and Tracer Compounds in Sweat, Saliva, and Plasma to Inform the Design of a Non-Invasive Wearable Sensor to Detect Medication Adherence

Source of Support:	NIH/NCI Experimental Therapeutics-Clinical Trials Network with Phase 1 Emphasis (ET-CTN) (UM1)
Principal Investigators:	W Zamboni
Total Direct Funding:	$26,540
Total Period of Support:	11/01/17 – 10/31/18
Percent Effort:	2% Effort / 2% Salary
Project Title:	Pharmacokinetic Analyses of 9922 as part of Phase 1/2 Clinical Trials of 9922

Source of Support:	1U54CA198999-01 – CCNE Pilot Grant
Principal Investigators:	Zamboni W
Total Direct Funding:	$49,885
Total Period Support:	08/01/17-10/31/18
Percent Effort:	5% effort/ 0% salary
Project Title:	Evaluation of nanoparticle drug delivery to tumors: Effects of Pharmacokinetic study design and metrics on delivery to tumors

Source of Support:	NCTraCs
Principal Investigators:	D Lawrence D
Total Direct Funding:	$15,839
Total Period of Support:	05/01/17 – 12/31/18
Co-Investigator:	W Zamboni
Percent Effort:	3% Effort / 3% Salary
Project Title:	Assay development and validation for quantitation of CY5-B12-docetaxel and photocleaved docetaxel + short chain in mouse plasma and tumors

Source of Support:	NIH / NCI (2-P30-CA016086)
Principal Investigators:	S Earp (PI of Pharmacology Core: W Zamboni)
Total Direct Funding:	$110,843/yr
Total Period of Support:	12/01/16 – 11/30/21
Percent Effort:	10% Effort / 10% Salary for Zamboni
Project Title:	Cancer Center Support Grant

Source of Support:	UNC Eshelman Institute for Innovation – Student/Postdoc Fellow
Principal Investigators:	A Lucas; W Zamboni (Advisor)
Total Direct Funding:	$25,000
Total Period of Support:	08/01/16 – 12/31/17
Percent Effort:	10% Effort / 0% Salary
Project Title:	Phenotypic Probe to Individualize the Treatment of Monoclonal Antibodies and Antibody Drug Conjugates

Source of Support:	Center for Translational Cancer Nanomedicine at Northeastern University
Principal Investigators:	W Zamboni

Total Direct Funding:	$14,000
Total Period of Support:	02/01/16 – 05/31/16
Percent Effort:	2% Effort / 2% Salary
Project Title:	ICP-MS Analysis of Platinum (Pt) in Blood, Kidney, Liver, Lung, and Heart as Part of the Study of Pharmacokinetic Analysis of Platinum Derivatives Following Systemic Administration in Mice

Source of Support:	1U54CA198999-01 – CCNE – Pilot Grant Program
Principal Investigators:	S Chang, W Zamboni
Total Direct Funding:	$50,000
Total Period of Support:	12/01/15 – 11/31/16
Percent Effort:	5% Effort / 0% Salary
Project Title:	Enhancing Tumor Delivery of Nanoparticle Anticancer Agents using Microbeam Radiation Therapy

Source of Support:	NIH R01 - 5R01CA184088-05
Principal Investigators:	A Kabanov (Lead PI), W Zamboni (Co-PI)
Total Direct Funding:	$1,494,965
Total Period Support:	12/01/2015 – 11/31/2020 (in NCE)
Percent Effort:	10% Effort/ 10% Salary
Project Title:	Liposomal Doxorubicin and Pluronic Combination for Cancer Therapy

Source of Support:	UNC LCCC Pilot Study
Principal Investigators:	D Darr, W Zamboni
Total Direct Funding:	$20,000
Total Period of Support:	10/01/15 – 09/30/16
Percent Effort:	0% Effort / 0% Salary
Project Title:	Analytical and PK studies of S1 in mice

Source of Support:	UNC Eshelman Institute for Innovation
Principal Investigators:	D Carpenter, A Sage, W Zamboni
Total Direct Funding:	$50,000
Total Period of Support:	10/01/15 – 09/30/16
Percent Effort:	5% Effort / 0% Salary
Project Title:	Creating the first non-invasive wearable technology to continuously monitor and improve patient medication adherence.

Source of Support:	1U01CA198910-01
Principal Investigators:	Kabanov, Bronich, Liu
Total Direct Funding:	$449,982
Total Period Support:	09/01/2015-8/31/2020 (in NCE)
Co-Investigator:	W Zamboni
Percent Effort:	10% effort/10% salary
Project Title:	Targeted Core Shell Nanogels for Triple Negative Breast Cancer

Source of Support:	1U54CA198999-01 - CCNE
Principal Investigators:	Huang (Contact PI) Project 4 PI: Kabanov
Total Direct Funding:	Project 4 $343,636
Total Period Support:	9/01/2015-7/31/2020
Co-Investigator:	W Zamboni
Percent Effort:	7% effort/ 7% salary
Project Title:	Nano Approaches to Modulate Host Cell Response for Cancer Therapy; Project 4 Title: High-Capacity Polymeric Micelle Therapeutics for Lung Cancer

Source of Support:	UNC Eshelman Institute for Innovation
Principal Investigators:	W Zamboni, S Chang
Total Direct Funding:	$50,000
Total Period of Support:	08/01/15 – 09/30/16
Percent Effort:	5% Effort / 0% Salary
Project Title:	Enhancing Tumor Delivery of Nanoparticle Anticancer Agents using Microbeam Radiation Therapy

Source of Support:	UNC Research Opportunity
Principal Investigators:	Lai S
Total Direct Funding:	$480,000
Total Period of Support:	07/01/15 – 06/30/18
Co-Investigator:	W Zamboni
Percent Effort:	0% Effort / 0% Salary (no salary allowed/requested)
Project Title:	Research Program in Immunoengineering

Source of Support:	NCSU College of Veterinary Medicine Pilot Grant
Principal Investigators:	M Risselada, K Messenger, W Zamboni
Total Direct Funding:	$11,930
Total Period of Support:	04/24/15 – 12/31/15
Percent Effort:	2% Effort / 2% Salary
Project Title:	Subcutaneous administration of carboplatin in pluronic F127 in a rodent model

Source of Support:	NIH 1R21EB017938-01
Principal Investigators:	S Lai
Total Direct Funding:	$125,000/yr x 2 yrs
Total Period of Support:	09/01/2014 – 08/31/16
Co-Investigator:	W Zamboni
Percent Effort:	5% Effort / 5% Salary
Project Title:	Prevalence and characteristics of anti-PEG antibodies in humans

Source of Support:	UNC LCCC Developmental Research Awards 2014
Principal Investigators:	W Zamboni
Total Direct Funding:	$50,000
Total Period of Support:	08/01/2014 – 07/31/2016
Percent Effort:	5% Effort / 0% Salary
Project Title:	Evaluation of Mediators of Mononuclear Phagocyte System (MPS) Function and Nanoparticle Pharmacology in Obese and Non-Obese Patients with Ovarian and Endometrial Cancer enrolled on the UNC Cancer Survivorship Cohort (CSC)

Source of Support:	NIH 1R21EB017938-01
Principal Investigators:	S Lai
Total Direct Funding:	$125,000/yr x 2 yrs
Total Period of Support:	09/01/2014 – 08/31/16
Co-Investigator:	W Zamboni
Percent Effort:	5% Effort / 5% Salary
Project Title:	Prevalence and characteristics of anti-PEG antibodies in humans

Source of Support:	UNC LCCC Developmental Research Awards 2014
Principal Investigators:	W Zamboni
Total Direct Funding:	$50,000
Total Period of Support:	08/01/2014 – 07/31/2016
Percent Effort:	5% Effort / 0% Salary

Project Title:	Evaluation of Mediators of Mononuclear Phagocyte System (MPS) Function and Nanoparticle Pharmacology in Obese and Non-Obese Patients with Ovarian and Endometrial Cancer enrolled on the UNC Cancer Survivorship Cohort (CSC)

Source of Support:	NIH/NCI Experimental Therapeutics-Clinical Trials Network with Phase 1 Emphasis (ET-CTN) (UM1).
Principal Investigators:	C Dees, H Hurwitz
Total Period of Support:	07/01/14 – 06/30/20
Co-Investigator:	W Zamboni (Director of Pharmacology Core)
Percent Effort:	1% Effort / 1% Salary

Source of Support:	The Ben and Catherine Ivy Foundation – Ivy Brain Tumor Program
Principal Investigators:	M Berens (PI of Pharmacology subcontract: W Zamboni)
Total Direct Funding:	$150,000
Total Period of Support:	07/01/14 – 06/30/16
Percent Effort:	5% Effort / 5% Salary
Project Title:	Delivery of Targeted Drugs Across the Blood Brain Barrier to Treat Glioblastoma

Source of Support:	U. S. FDA
Principal Investigators:	Y Cao
Total Direct Funding:	$460,000
Total Period of Support:	01/01/14 – 12/31/17
Co-Investigator:	W Zamboni
Percent Effort:	2% Effort / 2% Salary
Project Title:	Physiologically Based Pharmacokinetic Model for Drugs Encapsulated into Liposomes

Source of Support:	NIH / NCI (1 U54 CA151652-01) – Alliance Challenge Project (ACP)
Principal Investigators:	W Zamboni, A Kabanov
Total Direct Funding:	$55,000/yr
Total Period of Support:	07/01/13 – 04/30/15
Percent Effort:	2% Effort / 2% Salary for Zamboni
Project Title:	Pegylated Liposomal Doxorubicin (PLD) in Combination with Pluronic for Treatment of Ovarian and Breast Cancer

Source of Support:	Lilly Research Awards Program (LRAP)
Principal Investigators:	WC Zamboni
Total Direct Funding:	$98,000/yr x 1 yr
Total Period of Support:	06/01/13 – 05/31/15
Percent Effort:	10% Effort / 10% Salary
Project Title:	A High Throughput Screening Platform to Evaluate the Interactions between Nanoparticle and Non-Nanoparticle Agents and the Mononuclear Phagocyte System (MPS) in Humans and Animal Models

Source of Support:	Lilly Research Awards Program (LRAP)
Principal Investigators:	WC Zamboni
Total Direct Funding:	$98,000/yr x 1 yr
Total Period of Support:	06/01/13 – 05/31/15
Percent Effort:	10% Effort / 10% Salary
Project Title:	A High Throughput Screening Platform to Evaluate the Interactions between Nanoparticle and Non-Nanoparticle Agents and the Mononuclear Phagocyte System (MPS) in Humans and Animal Models

Source of Support:	NIH RO1 DA023690

Principal Investigators: L Tarantino, T Wiltshire
Total Period of Support: 03/01/13 – 06/30/18
Co-Investigator: W Zamboni
Total Direct Funding: $75,500/year
Percent Effort: 5% Effort / 5% Salary for Zamboni
Project Title: Organismal and Genetic Networks in Drug Reward and Reinforcement

Source of Support: NCI SBIR Phase II Grant: Multifunctional Therapeutics Based on Nanotechnology (N44CO-17019-36)
Principal Investigators: B Oberhardt (PI of Pharmacology subcontract: W Zamboni)
Total Direct Funding: $245,000
Total Period of Support: 09/28/12 – 09/27/14
Percent Effort: 5% Effort / 5% Salary
Project Title: NanoVector Phase II SBIR: Multifunctional Therapeutics using Engineered Plant Virus Nanoparticles
Source of Support: American Cancer Society Grant
Principal Investigators: CK Anders
Total Direct Funding: $100,000
Total Period of Support: 07/01/12 – 08/31/14
Co-Investigator/Mentor: W Zamboni
Percent Effort: 2% Effort / 2% Salary
Project Title: PARP Inhibition to Treat Triple-Negative Breast Cancer Brain Metastases

Source of Support: NC TraCS Pilot Grant
Co-Principal Investigators: C Anders, R Miller
Total Period of Support: 07/01/12 – 06/30/14
Co-Investigator: W Zamboni
Total Direct Funding: $50,000
Percent Effort: 0% Effort / 0% Salary for Zamboni
Project Title: Nanoparticle Anticancer agents for the Treatment of Metastatic Central Nervous System Malignancies

Source of Support: American Brain Tumor Association Discovery Grant
Principal Investigator: W Zamboni
Total Period of Support: 07/01/12 – 06/30/13
Total Direct Funding: $50,000
Percent Effort: 2% Effort / 2% Salary for Zamboni
Project Title: Nanoparticle Agents for the Treatment of Metastatic Central Nervous System Malignancies

Source of Support: NIH / NCI (1 U54 CA151652-01) – Alliance Challenge Project (ACP)
Principal Investigators: W Zamboni, P Decuzzi
Total Direct Funding: $40,000/yr
Total Period of Support: 07/01/12 – 06/30/13
Percent Effort: 5% Effort / 5% Salary for Zamboni
Project Title: A High Throughput Screening Platform with Mathematical Modeling to Evaluate the Interactions between Nanoparticle Agents and the Mononuclear Phagocyte System (MPS)

Source of Support: NIH K23
Principal Investigators: CK Anders
Total Direct Funding: $9,000
Total Period of Support: 09/01/11 – 08/31/13
Co-Investigator/Mentor: W Zamboni

Percent Effort:	0% Effort / 0% Salary
Project Title:	PARP Inhibition to Treat Triple-Negative Breast Cancer Brain Metastases

Source of Support:	NC TraCS 10KR101122
Principal Investigator:	G Song; W Zamboni
Total Direct Funding:	$10,000
Total Period of Support:	09/01/11 – 08/31/12
Percent Effort:	0% Effort / 0% Salary
Project Title:	Relationship between Monocytes Phagocyte System (MPS) in Tumors and Tumor Delivery and Efficacy of Nanoparticle Anticancer Agents in Genetically Engineered Mouse Models of Breast Cancer

Source of Support:	NIMH (1R01MH093372-01A1)
Principal Investigator:	B Philpot
Total Direct Funding:	$8,700
Total Period of Support:	09/01/11 – 08/31/12
Co-Investigator/Mentor:	W Zamboni
Percent Effort:	5% Effort / 5% Salary
Project Title:	Epigenetic Regulation of Ube3a as a Treatment for Angelman Syndrome

Source of Support:	NIH RO1 EB008733-01
Principal Investigator:	P Dayton
Total Period of Support:	03/01/11 – 02/28/14
Co-Investigator:	WC Zamboni
Total Direct Funding:	$57,500/yr x 2 yrs
Percent Effort:	7.5% Effort / 7.5% Salary
Project Title:	Precision Engineering of Ultrasonically-Targeted Drug Delivery Vehicles

Source of Support:	NIH / NIAID BAA-NIAID-DAIT-NIHAI2009060
Principal Investigators:	M Jay, R Mumper, W Zamboni
Total Direct Funding:	$4,563,828 (Total Grant Funding)
Total Period of Support:	09/30/10 – 09/29/13
Percent Effort:	10% Effort / 10% Salary for Zamboni
Project Title:	Development of Improved DTPA for Radionuclide Chelation – Phase IV.

Source of Support:	NIH / SAIC S10-155
Principal Investigators:	J Hrkach, WC Zamboni
Total Direct Funding:	$120,993
Total Period of Support:	09/01/10 – 08/31/11
Percent Effort:	5% Effort / 5% Salary
Project Title:	Pharmacologic Studies of BIND-Vincristine in Non-human Primates

Source of Support:	NIH / NCI (1 U54 CA151652-01)
Principal Investigators:	J DeSimone (PI of Pharmacology Core: W Zamboni)
Total Direct Funding:	$99,701
Total Period of Support:	09/01/10 – 08/31/15
Percent Effort:	10% Effort / 10% Salary for Zamboni
Project Title:	Carolina Center of Cancer Nanotechnology Excellence

Source of Support:	NC TraCS Institute
Principal Investigator:	W Caron; W Zamboni (Faculty Advisor)
Total Direct Funding:	$10,000
Total Period of Support:	07/01/10 – 06/31/11
Percent Effort:	0% Effort / 0% Salary

Project Title:	Development of an *Ex Vivo* Phenotypic Probe to Guide Pegylated Liposomal Doxorubicin (Doxil) Therapy in Patients

Source of Support:	NIH RO1 DA023690
Co-PIs:	L Tarantino, T Wiltshire
Total Period of Support:	07/01/09 – 06/30/11
Co-Investigator:	W Zamboni
Total Direct Funding:	$75,554/yr x 2 yrs
Percent Effort:	5% Effort / 5% Salary for Zamboni
Project Title:	Organismal and Genetic Networks in Drug Reward and Reinforcement

Source of Support:	PA-06-134 / NIAID Advanced Technology SBIR
Principal Investigators:	N Sharpless
Total Direct Funding:	$65,384
Total Period of Support:	04/01/09 – 03/31/10
Co-Investigator:	WC Zamboni
Percent Effort:	0% Effort / 0% Salary for Zamboni
Project Title:	G-Zero Therapeutics

Source of Support:	NIH/NCI CA119343 – CCNE Pilot Grant
Co-PIs:	William C. Zamboni; Paola Gehrig
Total Direct Funding:	$50,000
Total Period of Support:	01/01/09 – 12/31/11
Percent Effort:	0% Effort / 0% Salary
Project Title:	Carolina Center for Cancer Nanotechnology Excellence Pilot Grant: Study Evaluating Measures of the Reticuloendothelial System as Predictors of Doxil Pharmacokinetic and Pharmacodynamic Disposition in Patients with Refractory Ovarian Cancer

Source of Support:	UNC LCCC University Cancer Research Fund
Co-PIs:	W Zamboni; P Gehrig
Total Direct Funding:	$125,000
Total Period of Support:	01/01/09 – 12/31/10
Percent Effort:	5% Effort / 5% Salary
Project Title:	Study Evaluating Measures of the Reticuloendothelial System as Predictors of Doxil Pharmacokinetic and Pharmacodynamic Disposition in Patients with Refractory Ovarian Cancer

Source of Support:	NIH / NCI P42 Grant
Principal Investigator:	Jon Serody
Total Direct Funding:	$250,000
Total Period of Support:	12/01/08 – 12/01/10
Co-Investigator:	William C. Zamboni, Pharm.D., Ph.D.
Percent Effort:	0% Effort / 0% Salary
Project Title:	STTR Phase II Grant: Blockage of NF-Kappa B for Prevention/Treatment of GVHD

Source of Support:	NIH / NCI 3U54CA119343-05S2
Principal Investigators:	J DeSimone; W Zamboni
Total Direct Funding:	$74,500
Total Period of Support:	07/01/08 – 12/31/10
Percent Effort:	4% Effort / 4% Salary
Project Title:	Characterization of PRINT Nanoparticles Using SKOV-3 Mouse Model

Source of Support:	NIH / NIAID HHSN266200500045P
Co-PI:s	M Jay; W Zamboni; R Mumper

Total Period of Support:	07/01/08 to 09/29/09
Total Direct Funding:	$100,115/yr
Percent Effort:	12.5% Effort / 12.5% Salary
Project Title:	Development of Improved DTPA for Radionucleotide Chelation

Source of Support:	NIH / NIDDKD: Nanoscience and Nanotechnology in Biology and Medicine
Principal Investigator:	E Wiener
Total Period of Support:	07/01/07 to 08/30/12
Co-Investigator:	W Zamboni
Total Direct Funding:	$84,739/yr
Percent Effort:	10% Effort / 10% Salary
Project Title:	A New Dimension in Renal Clearance Design Criteria for Dendrimer Nanostructures

UNC – Past Contracts:

Source of Support:	Inimmune Pharma.
Principal Investigators:	Zamboni W
Total Direct Funding:	$75,000
Total Period of Support:	07/01/21 – 06/30/22
Percent Effort:	5% Effort / 5% Salary
Project Title:	Bioanalytical and Pharmacology studies of INI-4001 and INI-2004

Source of Support:	Meryx, Inc. (Task 5)
Principal Investigators:	Zamboni W
Total Direct Funding:	$65,000
Total Period of Support:	02/01/20 – 02/01/22
Percent Effort:	5% Effort / 5% Salary
Project Title:	Quantitation of MRX-2843 and Metabolites in Plasma in a Phase I Dose Escalation Study of the Safety, Pharmacokinetics, and Pharmacodynamics of MRX-2843 and Osimertinib in Adult Subjects with Relapsed/Refractory Leukemias

Source of Support:	Meryx (Tasks 1-4 and 6)
Principal Investigators:	Zamboni W
Total Direct Funding:	$254,598
Total Period of Support:	02/01/18 – 02/01/22
Percent Effort:	5% Effort / 5% Salary
Project Title:	Analytical and Pharmacokinetic Studies of MRX-2843 and metabolite(s) in Plasma and Urine as part of the Phase 1 Dose Escalation Study of the Safety, Pharmacokinetics and Pharmacodynamics of MRX-2843 in Adult Subjects with Refractory Solid Tumors

Source of Support:	OBI Pharma
Principal Investigators:	W Zamboni
Total Direct Funding:	$131,885
Total Period of Support:	06/01/20 – 12/31/21
Percent Effort:	5% Effort / 5% Salary
Project Title:	Measurement of the cell-associated exposures of human IgG1, Herceptin and OBI-898 (anti-SSEA-4 antibody) in circulating peripheral blood mononuclear cells by LC-MS/MS in patients with non-small cell lung cancer (NSCLC)

Source of Support:	ChemoGLO

Principal Investigators: Zamboni W
Total Direct Funding: $28,850
Total Period of Support: 03/01/17 – 03/31/21
Percent Effort: 2.5% Effort / 2.5% Salary
Project Title: Monoclonal antibody IgG1 quantitation from laboratory bench surfaces

Source of Support: NanoValent Pharmaceuticals, Inc.
Principal Investigators: W Zamboni
Total Direct Funding: $230,000
Total Period of Support: 06/01/20 – 05/31/21
Percent Effort: 5% Effort / 5% Salary
Project Title: Task#1: Preclinical characterization & evaluation of a targeted nanosphere formulation of CPT-11 (NV-103) by LC-MS/MS in mice to improve treatment of Ewing sarcoma as part of Pharmacologic development & evaluation of NV-103

Source of Support: Glolytics
Principal Investigators: Zamboni W
Total Direct Funding: $52,024
Total Period of Support: 08/01/17 – 07/31/18
Percent Effort: 5% Effort / 5% Salary
Project Title: Measure MPS Biomarkers in Blood as Part of Clinical Studies of MVT-5873

Source of Support: Glolytics
Principal Investigators: Zamboni W
Total Direct Funding: $75,218
Total Period of Support: 02/01/17 – 07/31/19
Percent Effort: 5% Effort / 5% Salary
Project Title: Evaluation of Function and Hormone Mediators of Mononuclear Phagocyte System (MPS) for MM-310-01-01-01 Study

Source of Support: Glolytics
Principal Investigators: Zamboni W
Total Direct Funding: $77,024
Total Period of Support: 02/01/17 – 01/31/19
Percent Effort: 5% Effort / 5% Salary
Project Title: Exploratory Analysis to Address Whether the Mononuclear Phagocyte System (MPS) Contributes to Faster Clearance of mAbs/ADCs in Advanced Gastric Cancer (AGC) Compared with Metastatic Breast Cancer (MBC) and Other Solid Tumors

Source of Support: ZY Therapeutics
Principal Investigators: Zamboni W
Total Direct Funding: $42,310
Total Period of Support: 02/01/17 – 06/30/17
Percent Effort: 3% Effort / 3% Salary
Project Title: Separation and quantitation of ZY-101 drug forms in rat plasma

Source of Support: NexImmune
Principal Investigators: W Zamboni
Total Direct Funding: $61,672
Total Period of Support: 08/01/15 – 03/31/16
Percent Effort: 5% Effort / 5% Salary
Project Title: Assay Development and Validation for Quantitation of Kb-SIY-dimer and anti-CD28 ligands in Solution for CMC Studies by High Resolution Mass Spectrometry (HRAM)

Source of Support:	Nemucore
Principal Investigators:	W Zamboni
Total Direct Funding:	$75,000
Total Period of Support:	07/01/14 – 06/30/16
Percent Effort:	5% Effort / 5% Salary
Project Title:	Development of Pt and Gd containing Nano-emulsions

Source of Support:	Merrimack Pharmaceuticals
Principal Investigators:	W. Zamboni
Total Direct Funding:	$53,823
Total Period of Support:	11/19/14 – 01/30/15
Percent Effort:	5% Effort / 5% Salary
Project Title:	Non-GLP development of analytical methods for MM-310 encapsulated and released drug - Task Order 2

Source of Support:	Onyx Pharmaceuticals
Principal Investigators:	W Zamboni
Total Direct Funding:	$125,820
Total Period of Support:	06/01/2014 – 05/31/15
Percent Effort:	5% Effort / 5% Salary
Project Title:	Evaluation of the pharmacodynamics, pharmacokinetics and efficacy of PEGylated liposomal carfilzomib and non-liposomal carfilzomib in female nu/nu mice bearing orthotopic A549 NSCLC tumors. The A549 NSCLC cells are luciferase expressing cell lines.

Source of Support:	Merrimack Pharmaceuticals
Principal Investigators:	W. Zamboni
Total Direct Funding:	$69,372
Total Period of Support:	05/15/14 – 08/01/14
Percent Effort:	5% Effort / 5% Salary
Project Title:	Non-GLP development of analytical methods for MM-310 encapsulated and released drug

Source of Support:	Hoffman-La Roche, Inc.
Principal Investigators:	J Shields, WC Zamboni
Total Direct Funding:	$35,000 ($17,500 for Zamboni)
Total Period of Support:	02/01/12 – 01/31/13
Percent Effort:	5% Effort / 5% Salary
Project Title:	Assessment of RO5212054/PLX3603 to 1) radiosenstize B-Raf mutant melanoma cells in vitro and 2) radiosensitize and/or inhibit melanoma brain tumor growth in vivo

Source of Support:	SciDose, LLC
Principal Investigators:	WC Zamboni
Total Direct Funding:	$97,994
Total Period of Support:	09/01/11 – 08/30/12
Percent Effort:	5% Effort / 5% Salary
Project Title:	Evaluation of the protein binding for novel formulations of Docetaxel

Source of Support:	Bayer HealthCare AG
Principal Investigators:	R Goldberg; WC Zamboni
Total Direct Funding:	$129,134
Total Period of Support:	02/01/11 – 07/01/14
Percent Effort:	10% Effort / 10% Salary

Project Title:	Pharmacokinetic Study of IHL=305 Alone and in Combination with Regorafenib as Part of the Placebo-Controlled Phase II Study of Regorafenib in Combination with FOLFIRI as Second-Line Therapy in Patients with K-RAS or BRAF Mutant Metastatic Colorectal Cancer
Source of Support:	Mallinckrodt/Covidien
Principal Investigators:	WC Zamboni
Total Direct Funding:	$196,910
Total Period of Support:	02/01/11 – 08/01/11
Percent Effort:	10% Effort / 10% Salary
Project Title:	Pharmacokinetic Screening of PEGylated Liposomal Formulations of Cisplatin in nu/nu Female Mice Bearing KB Human Nasopharyngeal Xenografts
Source of Support:	Mallinckrodt/Covidien
Principal Investigators:	WC Zamboni
Total Direct Funding:	$196,910
Total Period of Support:	02/01/11 – 08/01/11
Percent Effort:	10% Effort / 10% Salary
Project Title:	Pharmacokinetic Screening of PEGylated Liposomal Formulations of Cisplatin in nu/nu Female Mice Bearing KB Human Nasopharyngeal Xenografts
Source of Support:	SciDose, LLC
Principal Investigators:	WC Zamboni
Total Direct Funding:	$252,994
Total Period of Support:	10/01/10 – 09/30/11
Percent Effort:	7.5% Effort / 7.5% Salary
Project Title:	Pharmacology Studies of Curcumin-Succinate-PEG400 Conjugate compared with Curcumin In Vitro Systems and Tumor Models
Source of Support:	Mallinckrodt/Covidien
Principal Investigators:	WC Zamboni
Total Direct Funding:	$275,910
Total Period of Support:	07/01/10 – 05/30/11
Percent Effort:	10% Effort / 10% Salary
Project Title:	Efficacy and Pharmacology Studies of Folr1 Ab-SPI-077 compared with SPI-077 in Mice Bearing KB Human Nasopharyngeal Xenografts
Source of Support:	Carmel Pharma
Principal Investigators:	W Zamboni
Total Direct Funding:	$40,500/year
Total Period of Support:	05/01/10 – 04/30/15
Percent Effort:	2% Effort / 2% Salary
Project Title:	ChemoGLO Kits and Reference Laboratory for Chemotherapy Environmental Contamination in Pharmacies and Healthcare Areas
Source of Support:	Mersana Therapeutics, Inc.
Principal Investigators:	WC Zamboni
Total Direct Funding:	$221,332
Total Period of Support:	05/01/09 – 08/30/10
Percent Effort:	10% Effort / 10% Salary for Zamboni
Project Title:	Assay Development and LC-MS/MS Analysis as part of the Study Evaluating Plasma, Tissue, and Tumor PK of XMT-1001 and CPT-11 in Mice Bearing HT-29 Human Colon Carcinoma Xenografts
Source of Support:	Carmel Pharma

Principal Investigators: WC Zamboni
Total Direct Funding: $68,279
Total Period of Support: 05/01/09 – 04/30/10
Percent Effort: 2.5% Effort / 2.5% Salary for Zamboni
Project Title: Development of Wipe Sampling Kits, Methods, and Analytical Assays for Paclitaxel and Docetaxel as Related to Environmental Contamination in Pharmacies and Healthcares Areas

Source of Support: Hana Biosciences, Inc.
Principal Investigator: William C. Zamboni, PharmD, PhD
Total Direction Funding: $72,000
Total Period of Support: 05/01/08 – 5/01/10
Percent Effort: 15% Effort / 15% Salary Support
Project Title: Analytical Studies of Encapsulated, Released, and Sum Total Topotecan in Plasma as part of the Phase I Study of TLI

Source of Support: Sanofi-Aventis Oncology
Principal Investigators: R Edwards, K Zorn, WC Zamboni
Total Direct Funding: $125,000
Total Period of Support: 07/01/07 – 10/01/10
Percent Effort: 8% Effort / 8% Salary
Project Title: Parallel Phase I Studies of Docetaxel IV in combination with Oxaliplatin IP and Docetaxel IP in combination with Oxaliplatin IV in patients with Persistent or Recurrent Ovarian Cancer

Internal UNC Projects Administered Via Recharge Center – Past:

Source of Support: NINDS (R01NS097507)
Principal Investigator(s): Kristy Ainslie
Total Direct Funding: $3,084.32
Total Period of Support: 10/14/19– 04/14/20
Percent Effort: 1% Effort / 1% Salary
Project Title: Pharmacokinetic study of paclitaxel (PTX) in mouse brain via interstitial drug delivery (PTX scaffold)

Source of Support: UNC LCCC Development Grant
Principal Investigators: Hayes, Alyssa
Total Direct Funding: $50,000
Total Period Support: 02/01/21 to 12/31/22 (NCE)
Project Title: Pediatric Oncology Doxorubicin Implant

Source of Support: NIH 5R01AI162246-02 (PSID 5120650)
Principal Investigators: Rahima Benhabbour
Total Direct Funding: $1,496,202 current awarded; $3,740,241 Total award (5-year project)
Total Period Support: 04/13/2021 – 03/31/2026
Project Title: *Increasing tumoral drug uptake in pancreatic tumors using focused ultrasound and paclitaxel in-situ forming implants (UNC/NCSU BE - paclitaxel implant project)*

Source of Support: NCATS U01TR003715 (Account: 537210)
Principal Investigators: Hingtgen, Shawn (UNC); Floyd, Scott (Duke); Flores, Catherine (U. Florida)
Total Direct Funding: $2,999,304
Total Period Support: 04/01/2021 – 03/31/2025
Project Title: A consortium effort to translate therapies for neurological diseases via an ex vivo organotypic platform

University of Pittsburgh – Past Grants:

Source of Support:	Scaife Foundation Grant for Ovarian Cancer Research
Principal Investigator:	William C. Zamboni
Total Direct Funding:	$50,000
Total Period of Support:	09/01/06 – 05/01/08
Percent Effort:	5% Effort / 5% Salary
Project Title:	Pilot Study Evaluating Phenotypic Measures of the Reticuloendothelial System as Predictors of Doxil Pharmacokinetic and Pharmacodynamic Disposition in Patients with Refractory Ovarian Cancer

Source of Support:	NIH RO1 (Grant PI: Jennifer Grandis)
Co-Investigator:	W.C. Zamboni
Total Direct Funding:	$197,020
Total Period of Funding:	07/01/04 – 12/31/06
Percent Effort:	10% Effort / 10% Salary
Project Title:	Stat3 as a Therapeutic Target in Head and Neck Cancer

Source of Support::	Pittsburgh Foundation
Co-Investigator:	W.C. Zamboni
Total Direct Funding:	$24,319
Total Period of Funding:	07/01/04 – 06/30/06
Project Title:	The Role of Pharmacogenetics in Development of Individualized Chemotherapy for Women with Advanced Ovarian Cancer

Source of Support:	NIH
Principal Investigator:	Chandra Belani
Total Direct Funding:	$480,382
Total Period of Support:	12/01/01 – 11/30/06
Percent Effort:	2.5% Effort / 2.5% Salary
Project Title:	Phase I Clinical Trials of Novel Anticancer Agents

Source of Support:	ACCP– Aventis Oncology Fellowship
Principal Investigator:	William C. Zamboni
Total Direct Funding:	$30,000
Total Period of Support:	07/01/01 – 07/01/02
Percent Effort:	10% Effort / 0% Salary
Project Title:	Evaluation of Cisplatin Tumor Disposition Using Microdialysis in Patients with Melanoma.

Source of Support:	NIH, NCI
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$47,061
Total Period of Support:	04/01/01 - 03/30/02
Percent Effort:	5% Effort / 0% Salary
Project Title:	STTR Phase I Grant R41-CA91700: Potent Topoisomerase I inhibition by the Silatecan, DB-67

Source of Support:	The American Academy of Otolaryngology-Head and Neck Surgery Foundation
Principal Investigator:	Paul L. Leong
Total Direct Funding:	$6,000

Total Period of Support:	08/01/00 to 07/31/01
Percent Effort:	5% Effort / 0% Salary
Project Title:	Targeting Activated Stat3 in HNSCC

Source of Support:	Papa John's / V Foundation
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$5,000
Total Period of Support:	07/01/00 to 06/30/01
Percent Effort:	0% Effort / 0% Salary
Project Title:	Factors Affecting the Tumor Disposition of Anticancer

Source of Support:	NIH / NCI
Identification No.:	RFP NCI N01-CM-97019-58
Principal Investigator:	M.J. Egorin
Total Direct Funding:	$1,159,960
Total Period of Support:	12/1/99 to 12/01/04
Percent Effort:	10% Effort / 10% Salary
Project Title:	Preclinical Pharmacologic Studies of Antitumor Agents

Source of Support:	American College of Clinical Pharmacy and Rhone-Poulenc Rorer Pharmaceuticals Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$10,000
Total Period of Support:	7/1/99 to 6/30/00
Percent Effort:	10% Effort / 0% Salary
Project Title:	Disposition of Liposomal-Cisplatin (SPI-77) and Cisplatin in Solid Tumors

University of Pittsburgh – Past Contracts:

Source of Support:	Sanofi-Aventis Pharmaceuticals, Inc. (Grant PI: Dr. Levi Downs, Univ. of Minnesota)
Principal Investigator:	W.C. Zamboni, Pharm.D., Ph.D.
Total Direct Funding:	$35,658
Total Period of Support:	07/01/07 – 10/01/09
Percent Effort:	5% Effort / 5% Salary
Project Title:	LC-MS and Pharmacokinetics of Docetaxel as Part of Phase I Trial of Docetaxel as a Continuous IV infusion in Patients with Advanced Ovarian Cancer

Source of Support:	Hana Biosciences, Inc.
Principal Investigator:	William C. Zamboni
Total Direction Funding:	$84,441
Total Period of Support:	05/01/07 – 5/01/08
Percent Effort:	10% Effort / 10% Salary Support
Project Title:	Development of Sample Processing Methods and LC-MS Assay for the Measurement of Liposomal Encapsulated and Released Drug for Liposomal Topotecan in Human Plasma

Source of Support:	GlaxoSmithKline
Principal Investigator:	William C. Zamboni
Total Direct Funding:	$55,576
Total Period of Support:	10/01/06 – 10/01/07
Percent Effort:	15% Effort / 15% Salary
Project Title:	Pharmacokinetic Studies of Carboplatin Alone and In Combination with Lapatinib

Source of Support: ALZA Pharmaceuticals, Inc.
Principal Investigator: W.C. Zamboni
Total Direct Funding: $65,000
Total Period of Support: 04/01/06 – 04/01/07
Percent Effort: 10% Effort / 10% Salary
Project Title: Evaluation between the disposition of STEALTH liposomal CKD-602 (S-CKD602) and the Reticuloendothelial System in Preclinical Tumor Models

Source of Support: ALZA Pharmaceuticals, Inc.
Principal Investigator: W.C. Zamboni
Total Direct Funding: $50,000
Total Period of Support: 04/01/06 – 04/01/07
Percent Effort: 30% Effort / 30% Salary
Project Title: Pharmacokinetic Analysis of STEALTH liposomal CKD-602 (S-CKD602) as part of a Phase I Study

Source of Support: SuperGen Pharmaceuticals, Inc.
Co-Investigator: W.C. Zamboni
Total Direct Funding: $22,250
Total Period of Funding: 10/01/04 – 07/01/05
Percent Effort: 5% Effort / 5% Salary
Project Title: Disposition of 9NC and 9AC in Relation to ABC Genotypes

Source of Support: Sanofi-Aventis Pharmaceuticals, Inc.
Principal Investigator: Joe Kelly, M.D.
Co-Principal Investigator: W.C. Zamboni, Pharm.D., Ph.D.
Total Direct Funding: $66,850
Total Period of Funding: 07/01/04 – 06/30/09
Percent Effort: 15% Effort / 15% Salary
Project Title: The use of MDR1 and CYP Pharmacogenetic Variables in Designing Individualized Therapy for the Treatment of Ovarian Cancer

Source of Support: SuperGen Pharmaceuticals, Inc.
Co-Investigator: W.C. Zamboni
Total Direct Funding: $57,404
Total Period of Funding: 02/01/04 – 01/31/05
Percent Effort: 5% Effort / 5% Salary
Project Title: PK Analysis of 9NC and 9AC as Part of the Study Evaluating the Effect of Food on the Oral Absorption of Rubitecan

Source of Support: SuperGen Pharmaceuticals, Inc.
Co-Investigator: W.C. Zamboni
Total Direct Funding: $32,780
Total Period of Funding: 10/01/03 – 07/01/05
Percent Effort: 5% Effort / 5% Salary
Project Title: Bioequivalent Study of Two formulations of Rubitecan

Source of Support: Aventis and Sanofi Pharmaceuticals, Inc. (Grant PI: Jimmy Wong, MD, Georgetown University Cancer Ctr, Washington, DC)
Principal Investigator: W.C. Zamboni
Total Direct Funding: $85,600
Total Period of Support: 08/01/03 – 10/31/07
Percent Effort: 5% Effort / 5% Salary
Project Title: Phase I and Pharmacokinetic study of docetaxel and oxaliplatin

Source of Support:	Aventis Pharmaceuticals, Inc. (Grant PI: Marwan Fakih, MD Roswell Cancer Center, Buffalo, NY)
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$40,000
Total Period of Support:	04/01/03 – 10/01/07
Percent Effort:	5% Effort / 5% Salary
Project Title:	Phase I and Pharmacokinetic study of docetaxel, oxaliplatin, and cisplatin

Source of Support:	ALZA Pharmaceuticals, Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$245,000
Total Period of Support:	04/01/03 – 08/01/07
Percent Effort:	25% Effort / 25% Salary
Project Title:	Plasma, tissue, and tumor disposition of STEALTH liposomal and non-liposomal CKD602 in preclinical models

Source of Support:	ALZA Pharmaceuticals, Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$68,898
Total Period of Support:	04/01/03 – 07/01/07
Percent Effort:	12.5% Effort / 12.5% Salary
Project Title:	Phase I and pharmacokinetic study of STEALTH liposomal CKD602 in patients with refractory solid tumors

Source of Support:	Aventis Pharmaceuticals, Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$32,000
Total Period of Support:	04/01/03 – 10/01/05
Percent Effort:	5% Effort / 5% Salary
Project Title:	HPLC and Pharmacokinetics of Docetaxel as Part of Phase I Study of Docetaxel and Capecitabine in Patients with Solid Tumors

Source of Support:	Aventis Pharmaceuticals, Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$134,599
Total Period of Support:	03/01/03 – 08/01/07
Percent Effort:	15% Effort / 15% Salary
Project Title:	Plasma and tumor pharmacokinetics of EGFR AS oligonucleotide and docetaxel as part of the optimization of EGFR antisense oligonucleotides plus docetaxel for treatment of head and neck cancer

Source of Support:	Aventis Pharmaceuticals, Inc. (Grant PI: Dr. Yuhchyau Chen, Univ. of Rochester Medical Center)
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$30,000
Total Period of Support:	04/01/02 – 08/31/07
Percent Effort:	5% Effort / 5% Salary
Project Title:	HPLC and Pharmacokinetics of Docetaxel as Part of Phase II Study of Triple-Agent Chemotherapy Followed by Pulsed Radiosensitizing Docetaxel and Radiation for NSCLC

Source of Support:	Aventis Pharmaceuticals, Inc. (Grant PI: Kunle Odunsi, Roswell Cancer Center, Buffalo, NY)

Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$42,500
Total Period of Support:	04/01/02 – 08/31/07
Percent Effort:	7.5% Effort / 7.5% Salary
Project Title:	Pharmacogenetic, Pharmacologic, and Pharmacokinetic Study of Docetaxel as Part of Phase II Study of Weekly Docetaxel in Patients with Relapsed Ovarian Cancer

Source of Support:	Eli Lilly Pharmaceuticals, Inc. (Grant PI: Dr. Sridhar Mani, Montefiore University Hospital, NY, NY)
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$10,000
Total Period of Support:	04/01/02 – 03/31/02
Percent Effort:	5% Effort / 5% Salary
Project Title:	HPLC and Pharmacokinetics of Gemcitabine as Part of the Phase I Trial of Gemcitabine, Oxaliplatin, and 5FU in Patients with Solid Tumors

Source of Support:	Supergen Pharmaceutical Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$33,508
Total Period of Support:	11/1/99 to 11/30/01
Percent Effort:	5% Effort / 5% Salary
Project Title:	HPLC and Pharmacokinetic Analysis of 9-NC as Part of the Study Evaluating the Effect of Food on 9-NC Oral Absorption

Source of Support:	Rhone-Poulenc Rorer Pharmaceutical Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$156,863
Total Period of Support:	10/1/99 to 12/01/05
Percent Effort:	5% Effort / 5% Salary
Project Title:	Evaluating the Response and Pharmacokinetics of the Combination of Docetaxel and 9-NC in Mice Bearing Tumor Xenografts

Source of Support:	Supergen Pharmaceutical Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$60,616
Total Period of Support:	10/1/99 to 10/30/01
Percent Effort:	5% Effort / 5% Salary
Project Title:	HPLC and Pharmacokinetic Analysis of RFS2000 and its 9-AC Metabolite as Part of a Phase I Trial of RFS2000 in Patients with Refractory Solid Tumors

Source of Support:	Supergen Pharmaceutical Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$58,900
Total Period of Support:	7/1/99 to 6/30/01
Percent Effort:	10% Effort / 10% Salary
Project Title:	HPLC and Pharmacokinetic Analysis of RFS2000 and its 9-AC Metabolite as Part of a Phase II Trial of RFS2000 in Patients with Advanced Colo-Rectal Cancer

Source of Support:	Supergen Pharmaceutical Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$87,510
Total Period of Support:	7/1/99 to 6/30/00
Percent Effort:	15% Effort / 15% Salary

Project Title:	Evaluating the Relationship between Plasma Exposure of RFS2000 in Mice Bearing Human Colon Xenografts

University of Maryland Cancer Center – Past Grants:

Source of Support:	NIH, NCI
Identification No.:	1U01CA69854
Principal Investigator:	D. Van Echo
Annual Total Direct Cost:	$271,551
Total Period of Support:	3/1/98 to 2/28/03
Percent Effort:	15% Effort / 15% Salary
Project Title:	Phase I Trials of Anticancer Agents

Source of Support:	NIH, NCI
Identification No.:	REP NCI-CM-57199-12
Principal Investigator:	M.J. Egorin
Annual Total Direct Cost:	$172,429
Total Direct Funding:	$938,279
Total Period of Support:	3/1/98 to 11/30/99
Percent Effort:	20% Effort / 10% Salary
Project Title:	Preclinical Pharmacological Studies of Antitumor and Anti-HIV Agents

University of Maryland Cancer Center – Past Contracts:

Source of Support:	Sequus Pharmaceutical Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$47,061
Total Period of Support:	3/15/99 to 3/14/00
Percent Effort:	10% Effort / 0% Salary
Project Title:	Tumor Extracellular Fluid and Systemic Disposition of SPI-77 Alternative in Mice Bearing B16 Murine Melanoma Tumors

Source of Support:	Sequus Pharmaceutical Inc.
Principal Investigator:	W.C. Zamboni
Total Direct Funding:	$47,061
Total Period of Support:	3/1/99 to 2/28/00
Percent Effort:	10% Effort / 0% Salary
Project Title:	SPI-77 Tumor Extracellular Fluid and Systemic Disposition in Mice Bearing B16 Murine Melanoma Tumors

St. Jude Children's Hospital – Past Grants:

Source of Support:	ACCP, Rhone-Poulenc Rorer
Principal Investigator:	C. F. Stewart; W Zamboni
Total Direct Funding:	$22,000
Total Period of Support:	7/1/97 to 6/30/98
Percent Effort:	80% Effort / 75% Salary
Project Title:	Cerebrospinal Fluid Disposition of Topoisomerase I Inhibitors in the Nonhuman Primate Model

RESEARCH STATEMENT

Summary of Accomplishments (2012 to Present):

Scholarship. Since my promotion to Associate Profession with Tenure in January 2012, approximate 70% of my effort as a faculty member has been devoted to scholarship, with a focus on translational pharmacology studies and the translational development of drugs, especially complex drugs such as nanoparticles, conjugates, biologics, antibodies, and antibody drug conjugates.

My research program has several high impact areas of research that are as listed below:
1) Translational Pharmacology Studies of Nanoparticle, Carrier Mediated Agents (CMA), and Biologics
2) Biomarkers for the Bi-Directional Interaction between Carrier-Mediated Agents (CMA) and the Innate Immune System (IIS) / Mononuclear Phagocyte System (MPS)
3) Biomarkers for the Relationship between the Innate Immune System (IIS) / Mononuclear Phagocyte System (MPS) and Pharmacokinetics (PK) and Pharmacodynamics (PD) of Monoclonal Antibodies (mAbs) and Antibody Drug Conjugates (ADCs)
4) Profiling and Modulating Factors that Inhibit the Tumor Delivery of Carrier-Mediated Agents (CMAs) and Biologics
5) Evaluation and Removal of Surface Exposures of Hazardous Drugs in Hospitals.

The significance, innovation, impact, and summary of my publications for each of these areas of research are described below in the section entitled **Major Research Accomplishments**.

I serve as the director of the UNC Advanced Translational Pharmacology and Analytical Chemistry (ATPAC) Lab and Recharge Center in the UNC Eshelman School of Pharmacy (ESOP), the UNC Lineberger Comprehensive Cancer Center (LCCC), and the Carolina Institute of Nanomedicine. The UNC ATPAC Lab consists of the UNC Translational Oncology and Nanoparticle Drug Development Initiative (TONDDI) Lab and the UNC LCCC Analytical Chemistry and Pharmacology Core (ACPC) Lab. The UNC ATPAC Lab supports research from my own lab, and highly collaborative and team science-based research with faculty members in the UNC

ESOP, UNC LCCC, and CIN, as well as investigators from the National Institutes of Health, U.S. Food and Drug Administration, other academic research centers, and the pharmaceutical companies.

Summary of Research Program:

My research program is part of the Division of Pharmacotherapy and Experimental Therapeutics in the Eshelman School of Pharmacy at the University of North Carolina (ESOP). My research program is also part of UNC Lineberger Comprehensive Cancer Center (LCCC), and Carolina Institute of Nanomedicine (CIN). I am also the director of the UNC Advanced Translational Pharmacology and Analytical Chemistry (ATPAC) Lab. The UNC ATPAC Lab supports research from my own lab, and highly collaborative and team science-based research with faculty members in the UNC ESOP, UNC LCCC, and CIN, as well as investigators from the National Institutes of Health, U.S. Food and Drug Administration, other academic research centers, and the pharmaceutical companies. I consider myself as translational pharmacologists where I apply standard and novel analytical chemistry, pharmacology, pharmacokinetic, pharmacodynamic, and biomarker methods to preclinical, translational, and clinical development of drugs, especially anticancer agents.

I have been involved in translational development and pharmacology studies of small molecule drugs, nanoparticles, conjugates, biologics, and implantable agents for greater than 25 years. A majority of my work and interests has been on anticancer agents. My research interests focus on the application of pharmacokinetic, pharmacodynamic, phenotypic and pharmacogenetic principles in the optimization of the chemotherapeutic treatment of cancer. Information obtained from preclinical and clinical translational studies can greatly add to the understanding of the pharmacology of anticancer agents, allow for the rational design of therapeutic regimens, and permit individualization of treatment via precision medicine approaches.

A focus of my research is evaluating the processes and mechanisms associated with the delivery and distribution of anticancer agents into solid tumors. I am especially interested in identifying barriers to the delivery of agents into solid tumors and developing novel methods to measure these barriers. In addition, I am extremely interested into development novel technologies and modulators to overcome these barriers and increase the delivery and efficacy of anticancer agents in the treatment of solid tumors.

A second focus of my research is on the development of complex agents, such as nanoparticles, liposomes, conjugates, biologics, antibodies, and antibody drug conjugates (ADCs). As part of these studies, our group has developed methods and technologies to differentiate between the inactive-conjugated and active-released forms of these agents in blood, tumor, and tissues. I also focus on evaluating the bi-directional interaction between these agents and the mononuclear phagocyte system (MPS), which part of the innate immune system (IIS), and is the primary clearance pathway for these agents. We have developed biomarkers of the IIS/MPS, which can be used to predict the pharmacokinetics, pharmacodynamics, and the potential for drug-drug and drug-disease interactions of these complex agents, especially immune-oncology agents, antibodies, and nanoparticles. The IIS/MPS biomarkers are also being evaluated as a method to optimize the dose and regimen of these complex agents, in special populations, such as in obesity, inflammatory diseases, and COVID-19 infection.

In summary, the clinical relevance of my research is underscored by the need to optimize the selection of the best agent, dose, regimen, and combination therapies for the treatment of cancer and other diseases as a path to increase efficacy and reduce toxicities.

Laboratories:

I am the Director of the following laboratories at UNC Eshelman School of Pharmacy (ESOP) and UNC Lineberger Comprehensive Cancer Center (LCCC):

1) **Director, UNC Advanced Translational Pharmacology and Analytical Chemistry (ATPAC) Lab and Recharge Center**

   The UNC ATPAC Lab is a UNC Office of Sponsored Research approved recharge center that supports analytical chemistry and preclinical, translational, and clinical pharmacology studies with UNC and non-UNC investigators and institutions. The UNC ATPAC Lab consists of the following two labs with specific areas of research and support: 1) UNC Translational Oncology and Nanoparticle Drug Development Initiative (TOND$_2$I) Lab; 2) Analytical Chemistry and Pharmacology Core (ACPC) Lab. The UNC ATPAC Lab supports research from my own lab, and highly collaborative and team science-

based research with faculty members in the UNC ESOP, UNC LCCC, and CIN, as well as investigators from the National Institutes of Health, U.S. Food and Drug Administration, other academic research centers, and the pharmaceutical companies.

2) Director, UNC Translational Oncology and Nanoparticle Drug Development Initiative (TOND$_2$I) Lab in UNC ESOP and Carolina Institute of Nanomedicine (CIN)

The UNC TOND$_2$I Lab supports my personal academic research related to the translational development of anticancer agents with a focus on nanoparticle and carrier mediated agents and how these agents interact with the MPS. This lab also directly supports research Carolina Institute of Nanomedicine (CIN) and is a partner lab with the Nanomedicine Characterization Core Facility in the Center for Nanotechnology in Drug Delivery, UNC Eshelman School of Pharmacy, that is directed by Dr. Alexander Kabanov.

3) Director, Analytical Chemistry and Pharmacology Core (ACPC) Lab in UNC LCCC

This lab supports analytical chemistry, pharmacology and pharmacokinetic studies as related to preclinical and clinical drug development in the UNC LCCC.

As well as supporting my own research, the UNC ATPAC, UNC TOND$_2$I Lab and ACPC have and will support and collaborate on analytical and pharmacology projects for preclinical and clinical studies from several research groups and centers at UNC. The source of funding and projects associated with these studies are from the NIH, foundations, UNC, the State of NC, and pharmaceutical companies. A summary of the UNC and non-UNC groups collaborating with the TOND$_2$I Lab and UNC LCCC ACPC Lab are listed below:

1) UNC Eshelman School of Pharmacy (ESOP)
2) UNC ESOP Center for Integrative Chemical Biology and Drug Discovery (CICBDD)
3) UNC ESOP Center for Nanotechnology in Drug Delivery (CNBD)
4) UNC ESOP Institute for Pharmacogenomics and Individualized Therapy (IPIT)
5) UNC Carolina Center for Cancer Nanotechnology Excellence (CCCNE)
6) UNC School of Medicine (SOM)
7) UNC Chemistry Department
8) UNC LCCC
    a. Molecular Therapeutics
    b. Cancer Cell Biology
    c. Clinical Research
    d. Cancer Genetics
    e. Mouse Phase I Unit (MP1U)
    f. Developmental Therapeutics Program
    g. Phase I Program
9) NIH
    a. NCI
    b. NIAID
    c. NINDS
10) U.S. FDA
11) Other academic universities and cancer centers
12) Pharmaceutical Companies

TEACHING ACTIVITIES

Summary and Teaching Philosophy

My teaching role in the UNC ESOP has been and is to teach via didactic lectures, student advising, mentoring PharmD students on research projects [as part of the Research and Scholarship in Pharmacy (RASP), UNC ESOP Honors Program, and research internships in the UNC TOND$_2$I Lab], and advise PhD students and fellows and post docs.

My philosophy for didactic and experiential teaching is to stimulate the minds of the students so that they can become independent and creative thinkers. I want the students to be able to be make sound decisions and be creative in finding the answers to tough questions and situations, but more importantly also be able to ask the questions that are not being asked. I strongly feel that the most brilliant and successful people are not the people who find the answers but the people who find the next set of unanswered or unidentified questions. In order to do this a teacher must be able to stimulate and excite the students to be free thinkers.

Pharmaceutical sciences and the process of drug development is an ever-evolving area of research. Thus, pharmaceutical scientists need to have a wide range of knowledge but also have in depth knowledge of a specific area where they can become an expert. In order to educate and train the next generation of researchers a teacher must be able to communicate and facilitate a stimulating learning environment. I do this by not only lecturing to the students but also involving the students in the lecture via direct questions, problem solving paradigms, and real-life examples. In addition, I tie important information to clinical examples in an interactive exchange of information. For example, in my lecture on “Phases of Drug Development in Oncology” I highlight each important point with a discussion as if we (the class and I) were the directors of a pharmaceutical company and what decision(s) would we make based on available information presented in the lecture.

My teaching philosophy for student mentoring is to train PharmD and PhD students to become experts in the translational develop of anticancer agents, nanoparticles, conjugates, and biologics. In addition, a goal is to develop the students as creative, independent and self-directed investigators. I try to achieve this goal by providing students the opportunity to experience the studies, infrastructure, and methodologies required for this type of research. This is accomplished by including PhD and PharmD students, fellows, RASP students, honors students, and research interns as active members of our research program in the Translational Oncology and Nanoparticle Drug Development Initiative (TOND$_2$I) Lab. The more the students are involved and take charge of a project the more they are excited and energized by research and drug development. This is also a method to identify and recruit the best and brightest UNC students to our research program. This also results in a pipeline of outstanding students into the PhD and fellowship programs in the UNC ESOP. This process is already starting to produce results as several of our honors students and research interns are evaluating research careers and PhD and fellowship programs at UNC and other outstanding research institutions.

Accomplishments. I have used my teaching philosophy in my lectures to the PharmD students, PhD students, fellows, post docs, other trainees, and other medical professionals at UNC and throughout the U.S> and the world. The effectiveness of my teaching methods is highlighted in the outstanding reviews I have received in the course and lecture evaluations. In addition, I have extensive experience in mentoring fellows, post docs, PhD students and PharmD students as research interns and honors students. The students and trainees I have mentored have been highly successful in their programs at UNC and after leaving UNC. In addition, I have taken an active and administrative role in the Young Innovator Program (YIP) in the UNC Eshelman Institute of Innovation (EII), Honors Program, and RASP Program. Details on these accomplishments are included in the Teaching Portfolio section.

Teaching Activities:

University of North Carolina School of Pharmacy: 2008 - Present

UNC Didactic Courses:

Course Coordinator:

Co-Coordinator, Pharmacotherapy: Hematology and Oncology (PHCY 447) 2015
UNC Eshelman School of Pharmacy

Coordinator, Pharmacotherapy: Hematology and Oncology (PHCY 447) UNC Eshelman School of Pharmacy	2015
Co-Course Coordinator, Graduate Course in Science and Methods in Drug Development (DPET 841), UNC Eshelman School of Pharmacy	2013 - 2018
Co-Course Coordinator, Advanced Hematology and Oncology (DPET 812) UNC Eshelman School of Pharmacy	2010 - 2012

Lectures - Current:

Fundamentals of Research Study Design: Types of Studies, Endpoints, and Measurement Scales (RASP 1) UNC Eshelman School of Pharmacy, Chapel Hill, NC	2024 - Present
Introduction to the Institutional Review Board (IRB) (RASP 1) UNC Eshelman School of Pharmacy, Chapel Hill, NC	2024 - Present
Fundamentals of Data Analysis: Data Visualization (RASP 3) UNC Eshelman School of Pharmacy, Chapel Hill, NC	2024 - Present
Pharmacokinetics and Pharmacodynamics of Nanoparticle Agents Nanomedicine Graduate Course (MOPH 738) UNC Eshelman School of Pharmacy, Chapel Hill, NC	2009 - 2021 2024 – Present

Lectures - Past:

Non-clinical Safety Assessment of Drugs, Graduate Course in Science and Methods in Drug Development (DPET 841), UNC Eshelman School of Pharmacy	2014 - 2019
Oncologic Emergencies, Recitation Case Review, Hematology and Oncology (PHCY 447), UNC Eshelman School of Pharmacy	2014
Interspecies Scaling, Graduate Course in Pharmacokinetics (DPET 855) UNC Eshelman School of Pharmacy	2013 - 2019
Steps in the Preclinical and Clinical Development of Drugs UNC Eshelman School of Pharmacy Honors Program	2013 - 2014
Confirmatory Animal Pharmacology Studies, Graduate Course in Science and Methods in Drug Development (DPET 841), UNC Eshelman School of Pharmacy	2012 - 2019
Hematology and Oncology Recitation, Anemia Case Hematology and Oncology (PHCY 447), UNC Eshelman School of Pharmacy	2011 - 2015
Prostate Cancer, Pharmacotherapy: Hematology and Oncology (PHCY 447) UNC Eshelman School of Pharmacy	2011 - 2013
Hematology and Oncology Recitation, Breast Cancer Case Hematology and Oncology (PHCY 447), UNC Eshelman School of Pharmacy	2011 - 2013
Phases of Drug Development in Oncology, Advanced Hematology and Oncology (DPET 812), UNC Eshelman School of Pharmacy	2010 - 2017

Gynecologic Cancers, Pharmacotherapy: Hematology and Oncology (PHCY 447) UNC Eshelman School of Pharmacy	2010 - 2017
Translational Development of Anticancer Agents, Lunch and Learn Lecture Series in the UNC Graduate Training Program in Translational Medicine, UNC School of Medicine	2009 - 2010

UNC Training Courses

Lectures – Current:

Precision Dosing of Biologics Based on Body Habitus and Innate Immune System Factors UNC-Duke T32 Clinical Pharmacology Training Program UNC Eshelman School of Pharmacy, Chapel Hill, NC	2024
Effect of Body Habitus on the Precision Dosing of Complex Drugs and Biologics UNC ESOP Innovations and Transformations in Pharmaceutical Sciences (ITPS)	2023
Introduction to Clinical Pharmacology, NIH Principles of Clinical Pharmacology.	2019 - Present
Effect of MPS on Pharmacokinetics, Pharmacodynamics, and Tumor Delivery of Nanomedicines. Carolina Nanoformulations Workshop.	2018 - Present

Lectures – Past:

Conflict of Interest Cases in Academic Research, UNC ESOP Graduate Education Retreat	2020 - 2022
Bi-directional interaction between the innate immune system and complex drugs and biologics. UNC ESOP Innovations and Transformations in Pharmaceutical Sciences (ITPS)	2020 - 2022
Conflict of Interest Issues and Case in Academia, UNC Eshelman School of Pharmacy T32 Clinical Pharmacology Fellowship Program	2021
Lead Roundtable Discussion on Networking Skills in Research. DPET Graduate Students.	2017
Preclinical Characterization of ADME, PK, PD and toxicology of Nanoformulations; Use of nano agents in non-cancer diseases. Carolina Nanoformulations Workshop.	2016 - 2017
Factors affecting nano delivery to tumors in animal models and patients Clinical PK and PD (efficacy and toxicity) aspects of nano agents. Carolina Nanoformulations Workshop, UNC Eshelman School of Pharmacy.	2016 - 2017
Pharmacokinetics and Pharmacodynamics of Nanoparticles and Carrier-Mediated Agents in Preclinical Animal Models and in Patients, T32 Clinical Pharmacology Forum UNC Duke Collaborative Clinical Pharmacology Postdoctoral NIH T32 Training Program.	2015 - 2017
Course Coordinator and Developer, Steps and Methodology for the Translational Development of Nanoparticle Agents Carolina Center for Cancer Nanotechnology Excellence.	2011 - 2013

UNC Doctoral Student Major Advisor or Committee Chair

Gina Song, UNC Eshelman School of Pharmacy	2009 - 2014

-Primary Advisor
-Royster Society of Fellows Fellowship
-Globalization of Pharmaceutics Education Network (GPEN) 2012 Sponsored Graduate Student
Dissertation entitled "Immune Mechanisms Regulating Pharmacokinetics and Pharmacodynamics of PEGylated Liposomal Anticancer Agents".

Whitney Caron, UNC Eshelman School of Pharmacy — 2009 - 2013
- Primary Advisor
- American Foundation for Pharmaceutical Education (AFPE) Pre-Doctoral Fellowship in Pharmaceutical Sciences 2011
- St. Jude National Graduate Student Symposium (NGSS) – 2013
Dissertation entitled "The Mononuclear Phagocyte System as a Phenotypic Probe for Nanoparticle Pharmacokinetics and Pharmacodynamics in Preclincial and Clinical Systems".

Huali Wu, UNC Eshelman School of Pharmacy — 2008 - 2010
- Primary Advisor
Dissertation entitled "Clinical Pharmacokinetics and Pharmacodynamics of Anticancer Agents Delivered via PEGylated Liposomes".

Venita Gresham, UNC Eshelman School of Pharmacy — 2008 - 2010
- Committee Chair
Dissertation entitled "An Ex Vivo Familial Genetic Strategy For Determining Mechanism of Action".

UNC Thesis/Dissertation Committee Member

Zhongbo Li, PhD Committee, UNC Eshelman School of Pharmacy	2022 - Present
Rachel Cooke, PhD Committee, UNC Chemistry Department	2021 - Present
Sean McCann, PhD Committee, UNC Eshelman School of Pharmacy	2021 - 2022
Natasha Vinod, PhD Committee, UNC Eshelman School of Pharmacy	2018 - 2021
Christine Lee, PhD Committee, UNC Eshelman School of Pharmacy	2015 - 2020
Xiaomeng Wan, PhD Committee, UNC Eshelman School of Pharmacy	2015 - 2018
Nancy Gillis, PhD Committee, UNC Eshelman School of Pharmacy	2014 - 2017
Matthew Haynes, PhD Committee, UNC Eshelman School of Pharmacy	2014 - 2017
Hao Cai, PhD Committee, UNC Eshelman School of Pharmacy	2014 - 2016
Katherine Moga, PhD Committee, UNC Eshelman School of Pharmacy	2014 - 2015
Tammy Shen, PhD Committee, UNC Eshelman School of Pharmacy	2012 - 2014
James Huckle, PhD Committee, UNC Eshelman School of Pharmacy	2012 - 2014
Kevin Chu, PhD Committee, UNC Eshelman School of Pharmacy	2012 - 2013
Jessica Sorrentino, PhD Committee, UNC Pharmacology Department	2011 - 2013
Yong Zhang, PhD Committee, UNC Eshelman School of Pharmacy	2011 - 2013
Kai Chen, PhD Committee, UNC Chemistry Department	2011 - 2012
Dongyun Liu, PhD Committee, UNC Eshelman School of Pharmacy	2010 - 2013
Timothy Merkel, PhD Committee, UNC Chemistry Department	2010 - 2011
Lamar Mair, PhD Committee, UNC Applied Sciences and Engineering	2008 - 2012
Wesley Sivak, PhD Committee, University of Pittsburgh	2004 - 2007
Khalid Alkharfy, PhD Committee, University of Pittsburgh	2000 - 2002

UNC Fellowship Director and Advisor — 2008 - Present
Fellowship Program in Drug Development and Hematology and Oncology

UNC Eshelman School of Pharmacy, University of North Carolina

Li Chen, UNC Eshelman School of Pharmacy, Pharmacokinetics/Pharmacodynamics Fellow	2023 - 2024
Matthew Rich, CCCNE CCNTP Nano T32 Fellow -Co-mentor with William Polacheck, PhD, Joint Dept of Biomedical Engineering, UNC and NCSU -"Translational Studies of the Linear and Non-Linear Tumor Delivery of Nanoparticles and Small Molecules in Novel In Vivo and In Vitro Models of Solid Tumors"	2023 - Present
Taek Lee, UNC Eshelman School of Pharmacy, Pharmacokinetics/Pharmacodynamics Fellow	2022 - 2023
Jacob Ramsey, F99/K00 Fellow, Co-sponsor	2021 - Present
Amber Moody, CCCNE Nano T32 Fellow	2019 - 2021
Lauren Price, Hematology-Oncology Research Fellow, UNC Eshelman School of Pharmacy	2016 - 2018
Andrew Lucas, Hematology-Oncology Research Fellow, UNC Eshelman School of Pharmacy	2017 - 2017
Andrew Madden, Hematology-Oncology Research Fellow, UNC Eshelman School of Pharmacy	2012 - 2015
Linsey Phillips, UNC SPIRE Postdoc Program funded by NIGMS	2011 - 2014
Summit Rawal, Hematology-Oncology Research Fellow, UNC Eshelman School of Pharmacy	2011 - 2012
Parag Kumar, Drug Development Fellow UNC Eshelman School of Pharmacy	2011 - 2012
Jeff Huang, Drug Development Fellow UNC Eshelman School of Pharmacy	2010 - 2011
Mark Walsh, Hematology-Oncology Research Fellow, UNC Eshelman School of Pharmacy 2011 ASCO Oncology Trainee Award for study entitled "Technetium-99m sulfur colloid (TSC) as a phenotypic probe for the pharmacokinetics (PK) and pharmacodynamics (PD) of PEGylated liposomal doxorubicin (PLD) in patients (pts) with recurrent epithelial ovarian cancer (EOC)"	2009 - 2011
Austin Combest, Drug Dev. Fellow UNC Eshelman School of Pharmacy - 2010 AACR Sanofi-Aventis Scholar-in-Training Award for study entitled "Plasma and Tumor Pharmacokinetics (PK) of Carboplatin in Genetically Engineered Mouse Models of Melanoma (GEMMs), Murine Melanoma, and in Patients with Cutaneous Melanoma" - 2010 ASCO Cancer Foundation Merit Award for study entitled "Pharmacokinetics (PK) of oxaliplatin (OX) after Intravenous (IV) and intraperitoneal (IP) administration in patients with gynecological malignancies	2009 - 2010
Irene La, Hematology-Oncology Research Fellow, UNC Eshelman School of Pharmacy - 2009 Rho Chi Clinical Research Scholarship Awardee	2008 - 2010
Angela Yu, Drug Dev. Fellow, UNC Eshelman School of Pharmacy	2008 - 2009

<u>UNC School of Medicine Graduate Training Program in Translational Medicine Clinical Mentor</u>

Rachel Cooke Translational Development of Decodable Polymer Libraries for Protein Stabilization (PI: Abigail Knight, PhD)	2020 - 2023

<u>UNC ESOP RASP Students</u>

<u>RASP Faculty Mentor</u>

Reanna Jereb Crowed Bus Theory: PK Modeling of the Linear and Non-Linear Delivery of Nanoparticles in Preclinical Models of Solid Tumors	2021 - 2023

Sydney Stocks Preliminary Evaluation of the Effects of Body Habitus and Race on Pembrolizumab Response and Toxicity in Patients with Endometrial Cancer (Honors Carolina 2023)	2020 - 2023
William Bailey Burks Evaluation of the Effects of Body Habitus and Race on Pembrolizumab Response and Toxicity	2019 - 2020
Zachary Whitehead Effects of Obesity on the Efficacy of PEGylated Liposomal Doxorubicin in Patients with Platinum Refractory Ovarian Cancer (Honors Carolina 2021)	2018 - 2021

RASP Division Director

Melissa Roverse	2023 - Present
Sara Jubas	2023 - Present
Emily Ong	2023 - Present
Angela Su	2023 - Present
Allison Yang	2022 - Present
Melissa Maas	2022 - Present
Philip Quyang	2022 - Present
Ashley Gleaton	2021 - 2023
Brian Lam	2021 - 2023
Kelsey Chaykowski	2021 - 2023
Melanie Mills	2021 - 2023
J Bernard Collins	2020 - 2022
Monica Conzad	2020 - 2022
Taek Lee	2020 - 2022
Marissa Ross	2019 - 2021
Sarah Mills	2019 - 2021

UNC ESOP Research Honor Students or Independent Study Students

Esha Thakkar, Independent Study Student, UNC Eshelman School of Pharmacy Project entitled "Effect of Body Habitus on Bevacizumab Pharmacokinetics in Adult and Pediatric Patients with Refractory Solid Tumors"	2021 - 2023
Rachel Tyson, Research Honors Student, UNC School of Pharmacy Honors project entitled "Preclinical Development of Nanogel Formulations of Cisplatin"	2014 - 2018
Jeffery Roth, Research Honors Student, UNC School of Pharmacy Honors project entitled "Quantitation, Localization and Pharmacokinetics of Erlotinib Small Molecule and Nanoformulations in a GBM Mouse Model"	2014 - 2018
Leah Herity, Research Honors Student, UNC School of Pharmacy Honors project entitled "A High Throughput Screening Platform to Evaluate the Interactions between Nanoparticle and Non-Nanoparticle Agents and the Mononuclear Phagocyte System (MPS) in Humans and Animal Models"	2013 - 2017
Brittney Roberts, Research Honors Student, UNC School of Pharmacy	2013 - 2017

Honors project entitled "Evaluation of Mediators of Mononuclear Phagocyte System (MPS) Function and Nanoparticle Pharmacology in Obese and Non-Obese Patients with Ovarian and Endometrial Cancer enrolled on the UNC Cancer Survivorship Cohort (CSC)"

William McAdoo, Research Honors Students, UNC School of Pharmacy — 2012 - 2014
Honors project entitled "Modifying mononuclear phagocyte system in tumor to enhance the delivery of nanoparticle agents"

Amanda Keeler, Research Honors Student, UNC School of Pharmacy — 2011 - 2014
Honors project entitled "Pharmacokinetic, biomarker and pharmacodynamic studies of nanoparticle formulations of platinum analogues in the treatment of solid tumors and brain tumors"

Taylor White, Research Honors Student, UNC School of Pharmacy — 2011 - 2014
Honors project entitled "Profiling mononuclear phagocyte system in tumors: effects on clearance and tumor delivery of nanoparticle agents"

Andrew Lucas, Research Honors Student, UNC School of Pharmacy — 2010 - 2014
Honors project entitled "Sample processing and analytical methods to measure doxorubicin binding to DNA in biological samples"

Shane Moore, Research Honors Student, UNC School of Pharmacy — 2010 - 2013
Honors project entitled "Profiling the mononuclear phagocyte system (MPS) in solid tumors and the effects on nanoparticle tumor delivery"

Anthony Chhay, Research Honors Student, UNC School of Pharmacy — 2010 - 2012
Honors project entitled "Development of methods to count the number of nanoparticles in a dose and how this affects the PK and PD of the nanoparticle"

Ryan Schell, Research Honors Student, UNC School of Pharmacy — 2010 - 2012
Honors project entitled "Evaluation of inter-patient pharmacokinetic variability of liposomal and non-liposomal anticancer agents"

Hugh Giovinazzo, Research Honors Student, UNC School of Pharmacy — 2010 - 2012
Honors project entitled "Technetium-99m sulfur colloid as a phenotypic probe for the pharmacokinetics and pharmacodynamics of PEGylated liposomal doxorubicin (PLD)"

Katie Parise, Research Honors Student, UNC School of Pharmacy — 2009 - 2011
Honors project entitled "Comparison of toxicity and study design issues of nanoparticle and small molecule anticancer agents in preclinical models and phase I clinical trials."

Lakia Scoggins, Research Honors Student, UNC School of Pharmacy — 2008 - 2010
Honors project entitled "Evaluating the effects of bortezomib n the pharmacokinetics (PK) of pegylated liposomal doxorubicin"

UNC ESOP Research Interns

Angelia Stein, UNC — 2024 - Present
Corey Haswell, UNC — 2023 - Present
Claire O'Connor, UNC Eshelman School of Pharmacy — 2022 - Present
Kashish Patel, UNC Eshelman School of Pharmacy — 2022 - Present
Rowena Dzorvakpor, UNC Eshelman School of Pharmacy — 2022 - 2024
Alex Irmscher, UNC — 2021 - 2023
Alex Bean, UNC — 2021 - 2022
Mallory Storrie, UNC — 2019 - 2021
Hunter Hughes — 2021

Esha Thakkar, UNC Eshelman School of Pharmacy	2019 - 2021
Aaron Hamm, UNC	2019 - 2021
Taek Lee, UNC Eshelman School of Pharmacy	2018 - 2020
Natalie Huggins, UNC	2018 - 2019
Qiongqiong Mei, UNC Eshelman School of Pharmacy	2018 - 2019
Jisun Ban, UNC Eshelman School of Pharmacy	2017 - 2020
Emili Brooks Anderson, UNC	2017 - 2020
Jesse Lewandowski, UNC Eshelman School of Pharmacy	2017 - 2018
Juan Razo, UNC Eshelman School of Pharmacy	2016 - 2020
Savannah Megeau, UNC Eshelman School of Pharmacy	2016 - 2019
Joseph Piscitelli, UNC and UNC Eshelman School of Pharmacy	2015 - 2020
Amy Lin, UNC Eshelman School of Pharmacy	2015 - 2018
Leah Osae, UNC Eshelman School of Pharmacy	2015 - 2017
Zachary Kornblum, UNC Eshelman School of Pharmacy	2014 - 2017
Sarah Montgomery, Northwood High School	2014 - 2017
Fatimah Bori, UNC- North Carolina Central University Partners in Basic Cancer Research Intern Program	2013
Bernard Roles, Research Intern, NC State University	2013 - 2014
Candice Sherwood, Research Intern, UNC School of Pharmacy	2012 - 2014
Jennifer Coleman, Research Intern, UNC School of Pharmacy	2011 - 2013
Benjamin Guiastrennec, Res Intern, University of Montpellier, France Honors project entitled "Study of the Relationship between MPS Activity and the PK Disposition of Nanoparticle Formulations of Cisplatin in Tumors"	2011
Brian Sidone, Res Intern, Duquesne University School of Pharmacy, Pittsburgh	2011
Lavanya Rao, Research Intern, NC State University	2011
Elaine Yee-Ling, Research Intern, UNC School of Pharmacy	2010 - 2011
Whitney Davis, Research Intern, UNC School of Pharmacy	2010 - 2011
Katie Sandison, Research Intern, UNC School of Pharmacy	2009 - 2012
Ming Wu, Research Intern, UNC School of Pharmacy	2009 - 2010
Hiep C. Tu, Research Intern, UNC School of Pharmacy	2009 - 2010
Jeremy Sen, Research Intern, UNC School of Pharmacy	2009 - 2010
Vinh Hoang, Research Intern, UNC School of Pharmacy	2008 - 2011
Maureen Bottino, Research Intern, UNC School of Pharmacy	2008 - 2009
Elizabeth Neuffer, Research Intern, UNC School of Pharmacy	2008 - 2009
Xuefang Bai, Research Intern, UNC School of Pharmacy	2008 - 2009

UNC Eshelman Institute of Innovation Young Innovators Program (YIP)

Co-Faculty Director and Preceptor 2015 - 2018

YIP Students:

Jennifer Spores, Chapel Hill High School	2019
Alex Bean, Northwood High School	2019
Sara Eve, Northwood High School	2018

Megan Kanaby, Cardinal Gibbons High School	2018
Mallory Storrie, Northwood High School	2017
Hunter Hughes, Northwood High School	2017
Salem Williams, Northwood High School	2016

UNIVERSITY OF PITTSBURGH SCHOOL OF PHARMACY: 1999 - 2008

Didactic Courses:

Drug Development of Anticancer Agents, Elective Independent Study for P3 Students, School of Pharmacy, University of Pittsburgh — 2004 - 2008

Phase I and Phase II Study Designs in Oncology
Clinical Scientist-Ph.D. Program: School of Pharmacy
University of Pittsburgh, Pittsburgh, PA. — 2001 - 2008

Co-Course Coordinator, Principles of Clinical Pharmacology
Presented by National Institutes of Health
University of Pittsburgh, Pittsburgh, PA. — 2000 - 2001

Pharmacokinetics of Anticancer Agents, Pharmacotherapy:
Oncology and Hematology (Pharm 5315)
School of Pharmacy, University of Pittsburgh, Pittsburgh, PA. — 1999 - 2008

Drug Development in Oncology, Pharmacotherapy:
Oncology and Hematology (Pharm 5315)
School of Pharmacy, University of Pittsburgh, Pittsburgh, PA. — 1999 - 2008

Ovarian Cancer, Pharmacotherapy: Oncology and Hematology (Pharm 5315)
School of Pharmacy, University of Pittsburgh, Pittsburgh, PA. — 1999 - 2002

Comprehensive Chemotherapy Course: Plant Alkaloids: Taxanes,
Vinca Alkaloids, and Epipodophyllotoxins
University of Pittsburgh Cancer Institute, Pittsburgh, PA. — 1999 - 2002

Training Program

Co-Director of the Fellowship Program in Drug Development of Anticancer
Agents in Program of Molecular Therapeutics/ Drug Discovery
at University of Pittsburgh Cancer Institute. — 2000 - 2008

Fellowship Advisor

Laura Jung, Hematology-Oncology Research Fellow
University of Pittsburgh Cancer Institute — 2000 - 2003

DUQUESNE UNIVERSITY

Lectures:

Co-Course Coordinator, Pharmacotherapy: Hematology/Oncology
Duquesne University School of Pharmacy. — 2006 - 2008

UNIVERSITY OF MARYLAND

Lectures:

Clinical Pharmacokinetics of Chemotherapeutic Agents, Clinical Pharmacokinetics (PHMY-562), University of Maryland School of Pharmacy, Baltimore, MD.	1998 - 1999

Training Programs:

Co – Director Program in Oncology Pharmacy Research, Greenebaum Cancer Center and School of Pharmacy	1998 - 1999

UNIVERSITY OF TENNESSEE

Lectures:

Pharmacotherapeutics of Cancer Therapy Department of Clinical Pharmacy University of Tennessee College of Pharmacy, Memphis, TN.	1996 - 1997

PROFESSIONAL SERVICE

Current:

American Society of Clinical Oncology Annual Meeting Development Therapeutics & Cytotoxic Chemotherapy Committee	2020 - Present
American College of Clinical Pharmacy, Full Member	2001 - Present
American Association of Cancer Research, Active Member	1997 - Present
American Society of Clinical Oncology, Active Member	1997 - Present

Past:

NCI SBIR Special Emphasis Panel on Development of Cancer Therapeutics, Imagining Technologies, Interventional Devices, Diagnostics and Prognostics Toward Commercialization (R44)	2011 - 2017
NC Center of Innovation for Nanobiotechnology (COIN), Scientific Advisory Board	2010 - 2015
Drug Information Association Regulatory Affairs: The IND Phase	2009
University of Pittsburgh Alumni Association Board of Directors, Senior Advisor	2009 - 2011
American Society of Clinical Oncology 2006 Annual Meeting, Development Therapeutics & Cytotoxic Chemotherapy, Co-Chair of Oral Discussion Session	2006
Eastern Cooperative Oncology Group, Developmental Therapeutics Committee, Member	2005 - 2010
Gynecologic Oncology Group, Phase I and Pharmacology Committees, Member	2005 - 2010
American Society of Clinical Oncology 2005 Annual Meeting, Development Therapeutics & Cytotoxic Chemotherapy, Co-Chair of Poster Discussion Section	2005
American Society of Clinical Oncology, Development Therapeutics & Cytotoxic Chemotherapy, Member	2004 - 2010
Pennsylvania Cancer Control Consortium, Research Committee	2004 - 2007

University of Pittsburgh Alumni Association Board of Directors, Director-At-Large & Nominations Committee	2003 - 2008
University of Pittsburgh Board of Trustees, Athletics Committee, Faculty Representative	2003 - 2008
University of Pittsburgh Athletics Compliance Committee	2001 - 2008
University of Pittsburgh Athletics Advisory Committee on Admission of Student Athletes	2001 - 2008
University of Pittsburgh Alumni Association, Regional Director	2001 - 2003
University of Pittsburgh Senate Athletics Committee, Co-Chair	2000 - 2008
University of Pittsburgh Alumni Association, Board of Directors	1997 - 2008
University of Pittsburgh Alumni Association, Pitt Club Representative	1997 - 2001
University of Pittsburgh Memphis Area Pitt Organization, Alumni Leader	1995 - 1997
American College of Clinical Pharmacy, Associate Member	1994 - 2001
University of Pittsburgh School of Pharmacy Alumni Association	1994 - 1998
American Society of Health-Related Pharmacy	1993 - 1995
Rho Chi Pharmacy Honor Society, Secretary-Treasurer	1991 - 1992
Phi Delta Chi Fraternity	1989 - 1992

NIH STUDY SECTION PARTICIPATION

Past:

NCI SBIR Special Emphasis Panel on Development of Cancer Therapeutics, Imagining Technologies, Interventional Devices, Diagnostics and Prognostics Toward Commercialization (R44)	2010 - 2017
National Cancer Institute Nanotech Study Section	2009 - 2011
National Cancer Institute Development Therapeutics Study Section	2008 - 2009

ADVISORY COMMITTEE APPOINTMENTS

Current:

NuVeta Radiotherapy, Scientific Advisory Board, Durham, NC	2023 - Present
Member, Pharmaceutical Science and Clinical Pharmacology Advisory Committee of the US Food and Drug Administration, Silver Spring, MD	2022 - Present
Member, St. Jude Comprehensive Cancer Center Pharmacokinetic Shared Resource External Advisory Board, Memphis, TN	2022 - Present
Member, Champions Advisory Board, University of Pittsburgh Department of Athletics Pittsburgh, PA	2021 - Present
Deep Creek Pharma, Scientific Advisory Board, Winston Salem, NC	2021 - Present
Akagera Medicines, Scientific Advisory Board, Kigali, Rwanda	2020 - Present

Past:

Advisor, Cancer Nanotechnology Challenge	2015 - 2019
The Center for Advancing Innovation and Translation of Nanotechnology in Cancer (TONIC) Consortium	2014 - 2020

Advisor, Neuro Startup Challenge, The Center for Advancing Innovation	2014 - 2017
NanoEngineering for Medicine and Biology (NEMB) Workshop on Challenges for Engineers in Biomedical and Clinical Sciences	2012
NCI Alliance for Nanotechnology in Cancer: Animal Models Working Group, Co-Chair	2012 - 2020
NCI Alliance for Nanotechnology in Cancer Nanomedicine Drug Delivery Clinical Trial Working Group (NDD CTWR)	2012 - 2017
Pharmacologic and Regulatory Issues for the Translational Development of Nanoparticle Agents Workshop, Controlled Release Society Meeting 2011, Co-Chair	2011
Nanomedicine Product Development Summit: Turning Nanoparticle Delivery Systems into Innovative Medicines. Controlled Release Society Meeting 2011	2011
Controlled Release Society Educational Workshop entitled "Nanoparticle and Liposomal Regulatory and Pharmacology Issues", Co-Chair	2011
NCI Alliance for Nanotechnology in Cancer: Pharmacology and Biodistribution Working Group	2011 - 2020
NC Biomedical Innovation Network Symposium on Cutting-Edge Approaches to Drug and Device Development 2010, Co-Chair	2010
NC Center of Innovation for Nanobiotechnology (COIN) Scientific Advisory Board	2010 - 2013
Environmentally Responsible Development of Nanotechnology NC Summit	2009
NCI Best Practices in Cancer Nanotechnology Workshop	2009
NCI Alliance for Nanotechnology in Cancer, Pharmacology Committee	2009
Yakult Pharmaceutical Advisory Board	2008 - 2012
Neopharm, Inc., Liposomal Advisory Board	2006 - 2007
University Pharmacotherapy Associates	2004 - 2008
ALZA Inc., Oral Delivery Advisory Board	2002 - 2008
ALZA Inc., CDK602 Advisory Board	2002 - 2008
Amgen Inc., Oncology Advisory Board	2001 - 2005
Supergen Advisory Board	1998 - 2006
Optimized Analysis in Kinetics Consulting	1998 - 2000
SmithKline Beecham Regional Oncology Advisory Board	1998 - 1999

COMMITTEES

PROFESSIONAL ORGANIZATIONS (Including offices held)

Current:

ASCO Education Committee for Developmental Therapeutics and Tumor Biology	2019 - Present

Past:

12th International Symposium on Polymer Therapeutics: From Laboratory to Clinical Practice, Scientific Advisory Board	2018
American Association for Cancer Research Annual Meeting Program Committee	2014
Carolina Institute for NanoMedicine and Joint UNC-NC State BioMedical Engineering Dept. Conference, Core Development/Training Panel, Co-Chair	2012
Pharmacologic and Regulatory Issues for the Translational Development of Nanoparticle Agents Workshop	2011

Controlled Release Society Meeting, Co-Chair	
Symposium on Nanotechnology in Products: Pitfalls and Successes in the Path to a Commercial Product at the MANCEF/COMS Nanotechnology Meeting 2011, Greensboro, NC.	2011
Hematology Oncology Pharmacist Association, Research Committee	2010 - 2011
Southeastern Phase 2 Consortium (SEP2C), Pharmacology Committee	2009 - 2014
American Society of Clinical Oncology 2006 Annual Meeting, Development Therapeutics & Cytotoxic Chemotherapy, Co-Chair of Oral Discussion Session	2006
Eastern Cooperative Oncology Group, Developmental Therapeutics Committee, Member	2005 - 2017
Gynecologic Oncology Group, Phase I and Pharmacology Committees, Member	2005 - 2017
American Society of Clinical Oncology 2005 Annual Meeting, Development Therapeutics & Cytotoxic Chemotherapy, Co-Chair of Poster Discussion Section	2005
Pennsylvania Cancer Control Consortium, Research Committee	2004 - 2008
University of Pittsburgh Alumni Association	1992 - 2005
Rho Chi Pharmacy Honor Society, Secretary-Treasurer	1991 - 1992
Phi Delta Chi Professional Fraternity, Alumni Officer	1989 - 1992

UNIVERSITY AND SCHOOL

University of North Carolina:

Current:

UNC Eshelman School of Pharmacy, Conflict of Interest (COI) Committee, Lead Co-Chair	2023 - Present
UNC Eshelman School of Pharmacy DPET PK Metric Faculty Position Committee	2023
PharmAlliance Student Training Program – University College of London School of Pharmacy	2022
UNC Eshelman School of Pharmacy MMI PharmD Student Interview Committee	2022 - Present
J Heyward Hall Award Committee	2022 - 2023
UNC University Conflicts of Interest (COI) Advisory Committee	2020 - Present
UNC Eshelman School of Pharmacy, Conflict of Interest (COI) Committee, Co-Chair	2019 - 2022
UNC Eshelman School of Pharmacy RASP Committee	2018 - Present
NC TraCS Liaison from UNC Eshelman School of Pharmacy	2017 - Present
UNC Eshelman School of Pharmacy, Conflict of Interest (COI) Committee	2008 - Present

Past:

UNC Eshelman School of Pharmacy Research & Graduate Education Retreat Committee	2020 - 2022
UNC Eshelman School of Pharmacy Campbell Mentoring Program	2020 - 2022
UNC Technology-enable Clinical Services (TeCS) Company Commercialization Plan Committee	2020 - 2022
UNC Eshelman School of Pharmacy Accreditation Self-Study Committee: Standard 21 Sub-Committee	2018 - 2020
UNC Faculty Council, Tenured Representative for UNC Eshelman School of Pharmacy	2017 - 2019
UNC CFE Leadership Advanced Program	2017 - 2018
Eshelman Institute of Innovation (Eii), Review Committee for Student and Trainee Grant Proposals	2016 - 2017
Faculty Advisor for Dr. Eric Bachelder's KL2 Application	2015 - 2017
Carolina Nanoformulations Workshop, UNC Eshelman School of Pharmacy.	2015

UNC Eshelman School of Pharmacy, Faculty Search Committee for Clinical Scientist, Chair.	2014 - 2015
UNC Eshelman School of Pharmacy Curriculum Design and Execution Committee on Inquiry, Innovation and Problem Solving	2013 - 2017
UNC Eshelman School of Pharmacy Educational Renaissance – Scholarship Committee	2012 - 2013
UNC Eshelman School of Pharmacy ACPE Self-Study Committee on Administrative Relationships	2010
UNC LCCC Animal Studies Core Advisory Committee	2010 - 2019
UNC Eshelman School of Pharmacy Honors Program Committee	2010 - 2018
UNC Eshelman School of Pharmacy, DPET, PhD Qualifying Exam Committee	2010 - 2014
Faculty Advisor for Dr. Carey Anders' K23 Grant	2010 - 2014
Tgen / TD2 Drug Development Round Table	2009 - 2010
UNC Lineberger Comprehensive Cancer Center, Developmental Therapeutics Program, Clinical Pharmacology Co-Chair	2008 - 2020
UNC Lineberger Comprehensive Cancer Center, Mouse Phase I Unit Program, Co-Director	2008 - 2015
Committee on the Design and Implementation of the Phase I Unit of the UNC Lineberger Comprehensive Cancer Center in NCCH	2008 - 2009

University of Pittsburgh:

Protocol Review Committee, University of Pittsburgh Cancer Institute	2006 - 2008
University of Pittsburgh School of Pharmacy Admissions Committee	2006
University of Pittsburgh Alumni Association Board of Directors, Director at Large	2003 - 2008
University of Pittsburgh Board of Trustees, Athletic Committee	2003 - 2008
University of Pittsburgh Athletic Department Committee for NCAA Interim Report on Academic Integrity	2002
Pitt's Generation Next of the Metro Pitt Club, Chair	2002 - 2006
University of Pittsburgh Advisory Committee for the Admission of Student Athletes	2001 - 2008
University of Pittsburgh Alumni Association Board of Directors, Regional Director	2001 - 2003
University of Pittsburgh Faculty Senate	2000 - 2008
Senate Athletics Committee, Co-Chair	
University of Pittsburgh Alumni Association Board of Directors, Scholarship Committee	1997 - 2017
Chair	2001 - 2015
University of Pittsburgh Alumni Association Board of Directors, Pitt Club Representative	1997 - 2001

CONSULTANT

Current:

Genentech	2024 - Present
Ingenus Pharmaceuticals	2024 - Present
NuVeta Radiotherapy	2023 - Present
Inimmune	2021 - Present
Akagera Medicines	2020 - Present
GlaxoSmithKline	2020 - Present
Syros Pharmaceuticals	2017 - Present

Glolytics, LLC, Co-Founder and CSO	2016 - Present
ChemoGLO, LLC, Co-Founder and CSO	2012 - Present
MediGLO Pharmaceutical Consulting, LLC, Founder and CEO	2002 - Present

Past:

Glycomine	2022 - 2024
Gilead Sciences	2022 - 2024
Eagle Pharmaceuticals	2020 - 2022
Adaptimmune Therapeutics	2021 - 2022
Ellipses Pharma	2020
OBI Pharmaceuticals	2018 - 2020
BlueLink Pharmaceuticals	2017 - 2020
Cerulean Pharma	2016 - 2017
NuVue	2016 - 2017
Cristal Therapeutics, Scientific Advisory Board	2015 - 2016
Mallinckrodt Pharmaceuticals, Scientific Advisory Board	2015 - 2015
Wildcat-Nanoglo, LLC, Co-Founder; Chair of Scientific Advisory Board	2014 - 2015
Merrimack Pharmaceuticals	2013 - 2019
Nanovector, Scientific Advisory Board	2012 - 2016
Onyx Pharmaceuticals	2012 - 2015
Nektar Therapeutics	2012 - 2013
AZAYA Therapeutics	2011 - 2012
Covidien-Mallinkrodt	2010 - 2013
Terumo Corporation	2010 - 2012
Endece	2010 - 2011
Aura Biosciences	2010 - 2011
Guide Point Global Consulting	2009 - 2012
Liquidia	2009 - 2010
Yakult Pharmaceuticals	2008 - 2010
Genentech	2008 - 2009
Enzon Pharmaceuticals	2008 - 2009
Labopharm	2008 - 2009
Hana Biosciences	2007 - 2009
Clinical Advisors, Network of Advisors Consulting	2006 - 2009
MEDACorp, Medical Consulting	2006 - 2009
Neopharm, Inc.	2006 - 2007
Alza Corp.	2002 - 2008
Amgen Inc. Oncology Advisory Board	2001 - 2005
Supergen Advisory Board	2000 - 2008
SmithKline Beecham Regional Oncology Advisory Board	1998 - 1999
Optimized Analysis in Kinetics Consulting	1998 - 1999

REVIEWER

Journal Reviewer

Reviewer, American Journal of Health-System Pharmacy	2022 - Present
Reviewer, PNAS	2015 - Present
Reviewer, Journal of Oncology Pharmacy Practice	2014 - Present
Reviewer, Advanced Drug Delivery Reviews	2012 - Present
Reviewer, International Journal of Pharmaceutics	2012 - Present
Reviewer, Journal of Liposomal Research	2009 - Present
Reviewer, Journal of Pharmacology and Experimental Therapeutics	1999 - Present
Reviewer, Journal of Clinical Oncology	1999 - Present
Reviewer, Clinical Cancer Research	1998 - Present
Reviewer, Cancer Chemotherapy and Pharmacology	1996 - Present

Editorial Advisory Board

Editorial Board Member, Drugs of the Future	2009 - 2023

Other

Medical Writer for Oncology, Medscape, Inc.	1999 - 2001

EXHIBIT 11

ACCORD'S WITNESS LIST

UNREDACTED PUBLIC VERSION

HIGHLY CONFIDENTIAL –
SUBJECT TO PROTECTIVE ORDER

ACCORD'S WITNESS LIST

1. Accord reserves the right to call substitute witnesses to the extent that a witness's circumstances change, or a witness otherwise becomes unavailable for trial. Accord further reserves the right to call any witness for impeachment purposes.

2. Accord also reserves the right to call any witness listed on Plaintiff's witness lists.

3. Accord reserves the right to call one or more witnesses not identified below whose testimony is necessary to establish the admissibility of a trial exhibit if the admissibility of the exhibit is challenged by Plaintiff.

4. By identifying these witnesses, Accord is not required to call them at trial, nor is Accord limited in the manner in which such testimony is presented at trial.

5. The following is a list of fact witnesses whose testimony Accord will present at trial by deposition:

Ajeet Singh
Bandu Nagaraju
Kocherlakota Chandrashekhar

6. The following is a list of expert witnesses whose testimony Accord will present live at trial: Dr. Jason McConville.

EXHIBIT 12

UNREDACTED PUBLIC VERSION

CURRICULUM VITAE
Jason T. McConville, Ph.D.
Associate Professor of Pharmaceutics

Mailing Address:
Department of Pharmaceutical Sciences, University of New Mexico,
College of Pharmacy, 2705 Frontier Avenue NE, Albuquerque, NM 87131.

Electronic mail: jmcconville@unm.edu
Telephone: +1 (505) 925-4446; Facsimile: +1 (505) 925-4549

I. Personal

Born July 13, 1971 in Coventry, United Kingdom.
Married.

Citizen of The United Kingdom of Great Britain and Northern Ireland.
Citizen of The United States of America.

II. Education

Oct 91 – Jun 94	Bachelor of Science with Honors, Applied Chemistry Coventry University, Coventry, United Kingdom
Jul 99 – Sep 02	University of Strathclyde, Glasgow, United Kingdom. Doctor of Philosophy, Pharmaceutics
Dissertation:	“Pulsed-Release Drug Delivery and Development of the Time-Delayed Capsule”

III. Positions Held

September 1994 to July 1999 –Research Technician in Pharmaceutics,
Centre for Drug Formulation Studies, University of Bath, Bath, United Kingdom.

July 1999 to September 2002 – Ph.D. Student/Candidate,
Department of Pharmacy, University of Strathclyde, Glasgow, United Kingdom.

October, 2002 to August 2006 – Post Doctoral Fellow/ Research Associate,
College of Pharmacy, University of Texas at Austin, Austin, TX.

August, 2006 to May 2012 – Assistant Professor of Pharmaceutics,
College of Pharmacy, University of Texas at Austin, Austin, TX.

July, 2012 to Present – Associate Professor of Pharmaceutics,
College of Pharmacy, University of New Mexico, Albuquerque, NM.

August, 2012 to Present – Adjunct Professor
Department of Pharmaceutical Technology and Biopharmacy,
University of Bonn, Germany.

July, 2021 to Present – Vice Chair of Education in Pharmaceutical Sciences,
College of Pharmacy, University of New Mexico, Albuquerque, NM.

IV. Professional Memberships

American Association of Pharmaceutical Scientists *Sections: Formulation Design & Development* *Physical Pharmacy & Biopharmaceutics*	1997 - present
Aerosol Society	1997 - present
Controlled Release Society	2002 – present
Canadian Society for Pharmaceutical Sciences	2004 – present
American Association of Colleges of Pharmacy	2006 – present
American Association of Pharmaceutical Scientists *Inhalation and Nasal Community Leadership Member*	2020 - present

V. Professional Training

Short course: *Particle Characterization using Low Angle Laser Light Scattering*,
Malvern Instruments, Limited, Malvern, Worcestershire, UK, June, 1996.

The Royal Institute of Biology, *Accredited Training for Personnel Working under the Animals (Scientific Procedures) Act 1987* (Modules 1, 2, 3, and 4),
Guy's, King's and St Thomas' Medical School, London, UK, April, 1997.

Short course: *Advances in Controlled Release and Drug Delivery Technologies*.
The Center for Microencapsulation and Drug Delivery, Texas A&M University,
College Station, TX, October, 2004.

Short course: *Particle Engineering Technologies: Theory and Practice*,
American Association of Pharmaceutical Scientists, Baltimore, MD, November, 2004.

Short course: *Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist*,
University of Minnesota, College of Pharmacy, Minnesota, MN, July, 2005.

Workshop: *Tablet Coating Technologies*, *International Pharmaceutical Excipients Council (IPEC Americas 2008)*, San Juan, Puerto Rico, April, 2008.

The Royal Institute of Biology, *Accredited Training for Personnel Working under the Animals (Scientific Procedures) Act 1987* (Modules 1, 2, 3, 4, and 5), Vesalius, London, UK, June, 2009.

Joint American Association of Pharmaceutical Scientists/Controlled Release Society Workshop: *Developing Pharmaceutical Products for Controlled Pulmonary Delivery*, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington, DC, October, 2011.

Workshop: *Setting Release Specifications for in vitro Testing of Controlled Release Dosage Forms*, 39th International Symposium on Controlled Release of Bioactive Materials, Quebec City, Canada, July, 2012.

Short Course: *Macromolecule Drug Delivery: Challenges and Triumphs*, AAPS National Biotechnology Conference, San Diego, CA, May, 2014.

National Association for Biomedical Research (NABR), Reducing Burden: Options and Opportunities, November, 2017.

Collaborative Institutional Training Initiative, Planning Research and Completing the Protocol Form, December, 2018.

Office of Laboratory Animal Welfare (OLAW), 21st Century Cures Act, December, 2019.

VI. Current Research Interests

New technologies to improve patient compliance and health outcomes with inhalation, oral, thin film, and 3D printed drug delivery technologies.

VII. Honors and Awards

1. Annual Research Day Award for "Design and Evaluation of Pulsatile Drug Delivery Capsule", *University of Strathclyde*, Glasgow, May, 2001.

2. Outstanding Presentation Award: "Microwave Dielectric Analysis of Wet Granulations for Erodible HPMC Tablets", *138th British Pharmaceutical Conference*, Glasgow, United Kingdom, September, 2001.

3. Editor's Choice Award: "Design and Evaluation of a Restraint-Free Small Animal Inhalation Dosing Chamber". *LeadDiscovery*, February, 2005.

4. Innovative Aspects of Oral Drug Delivery and Absorption Graduate/Post-Doc Award: "Improved Dissolution Rate and Bioavailability through the Formation of a Highly Miscible Binary Mixture", *32nd International Symposium on Controlled Release of Bioactive Materials*, Miami, FL, June, 2005.

5. Best Resident and Research Presentation Award: "Aerosolized Itraconazole (ITZ) as Prophylaxis against Invasive Pulmonary Aspergillosis (IPA) due to *Aspergillus fumigatus*", *27th American College of Clinical Pharmacy Annual Meeting*, St. Louis, MS, October, 2006.

6. Invited article: J.T. McConville, N.P. Wiederhold, Antifungal Prophylaxis to the Lung Using Itraconazole, *Inhalation*, 1(2007) 6-9.

7. Invited article: J.T. McConville, Targeted Lung Delivery of Antifungals: Preclinical Studies Using Itraconazole Nanoparticles, *RDD Europe 2007*, 1(2007) 43-50.

8. Invited article: D.A. Miller, J.T. McConville, W. Yang, R.O. Williams III, J.W. McGinity, Hot-Melt Extrusion for Enhanced Delivery of Drug Particles, *Journal of Pharmaceutical Sciences*, 96(2007) 361-76. Invited Article.

9. Featured News Article: "University of Texas at Austin Pharmacy Researcher Works to Lower Carbon Footprint of Pharmaceuticals", *www.BiobasedNews.com*, August, 2008.

10. Featured News Article in Carbon Market News: "Research Reveals Pharmaceuticals Can Cut Carbon Footprint with Organic Solvent", *www.carbonoffsetsdaily.com*, August, 2008.

11. Guest Editor: Innovative Inhalation Technologies: Special Edition: *Drug Development and Industrial Pharmacy*, 34(2008).

12. Invited article: Y-J. Son, J.T. McConville, Advancements in Dry Powder Delivery to the Lung, Special Edition: Innovative Inhalation Technologies, *Drug Development and Industrial Pharmacy*, 34(2008) 948-959.

13. Invited article: A.B. Watts, J.T. McConville, R.O. Williams III, Current Therapies and Technological Advances in Aqueous Aerosol Drug Delivery, Special Edition: Innovative Inhalation Technologies, *Drug Development and Industrial Pharmacy*, 34(2008) 913-922.

14. Invited article: W. Yang, J. Tam, D.A. Miller, J. Zhou, J.T. McConville, K.P. Johnston, R.O. Williams III, High Bioavailability from Nebulized Itraconazole Nanoparticle Dispersions with Biocompatible Stabilizers, Special Edition: Pharmaceutical Nanotechnology, *International Journal of Pharmaceutics*, 361(2008) 177–188.

15. Session Judge: Poster on the Podiums, *Respiratory Drug Delivery (RDD2008)*, Scottsdale, Arizona, 2008.

16. Research Presentation Award: "Manufacture and Characterization of Natural Polymer Based Films as Buccal Delivery Systems", *International Pharmaceutical Excipients Council (IPEC Americas 2009)*, San Juan, Puerto Rico, April, 2009.

17. Invited article: S. Thitinan, J.T. McConville, Interferon Alpha Delivery Systems for the Treatment of Hepatitis C, *International Journal of Pharmaceutics*. 369(2009) 121-135.

18. Invited article: J.T. McConville, S.A. Kucera, T.C. Carvalho, E.M. Hurley, Ethyl Lactate as a Pharmaceutical-Grade Excipient and Development of a Sensitive Peroxide Assay, *Pharmaceutical Technology*, 33(2009) 74-84.

19. Invited article: Y-J Son, J.T. McConville, Dissolution Testing for Inhalation Formulations, *Inhalation*, 2:6(2009) 8-11.

20. Invited article: Y-J. Son, M. Horng, M. Copley, J.T. McConville, Optimization of an *In Vitro* Dissolution Test Method for Inhalation Formulations, *Dissolution Technologies*, 17(2010), 6-13.

21. Member of the Society for Teaching Excellence, *University of Texas at Austin*, September, 2011.

22. Corresponding author for the most downloaded article in *European Journal of Pharmaceutics and Biopharmaceutics*: "Manufacture and Characterization of Mucoadhesive Buccal Films", January-March 2011.

23. Invited article: T.C. Carvalho, S.R. Carvalho, J.T. McConville, Formulations for Pulmonary Administration of Anticancer Agents to Treat Lung Malignancies, *Journal of Aerosol Medicine and Pulmonary Drug Delivery*, 24 (2011), 61-80.

24. Nomination: University of Texas System Regents' Outstanding Teaching Award, December 2011.

25. Research Presentation Award: Influence of particulate API in Eudragit® RS and RL films for buccal delivery, *International Pharmaceutical Excipients Council (IPEC Americas 2012)*, San Juan, Puerto Rico, 2012.

26. Invited article: S. Thitinan, J.T. McConville, Development of a Gastroretentive Pulsatile Drug Delivery Platform, *Journal of Pharmacy and Pharmacology*, 64 (2012), 505-516.

27. Invited article: Y-J. Son, J.T. McConville, Preparation of Sustained Release Rifampicin Microparticles for Inhalation, Special Edition: *Journal of Pharmacy and Pharmacology*, 64 (2012), 1291-1302.

28. Research Presentation Award: "Antisolvent Co-Precipitation Synthesis of D,L-Valine/Lysozyme", *International Pharmaceutical Excipients Council (IPEC Americas 2014)*, Raleigh-Durham, NC, April, 2014.

29. Invited article: J.O. Morales, J.T. McConville, Novel Strategies for the Buccal Delivery of Macromolecules, *Drug Development and Industrial Pharmacy*, 40 (2014), 579–590.

30. Best Inter-Departmental Collaborative Research Award: "Polymeric Coating of Endotracheal Tubes for Local Drug Delivery", *University of New Mexico College of Pharmacy Research and Scholarship Day*, Albuquerque, NM, September, 2015.

31. Invited article: J.E. Hasted P. Bäckman, A.R. Clark, W. Doub, A. Hickey, G. Hochhaus, P.J. Kuehl, C-M. Lehr, P. Mauser, J. McConville, R. Niven, M. Sakagimi and J.G. Weers, Scope and relevance of a pulmonary biopharmaceutical classification system AAPS/FDA/USP Workshop March 16-17th, 2015 in Baltimore, MD, *AAPS Open*, 2 (2016), 1-20.

32. Invited article: T.C. Carvalho, J.P. McCook, N.R. Narain, J.T. McConville, Development of Aqueous Dispersions of Coenzyme Q10 for Pulmonary Delivery and the Dynamics of Active Vibrating-Mesh Aerosolization, Special Issue: Staniforth Festschrift, *International Journal of Pharmaceutics*, 514 (2016), 514(2), 407-419.

33. Invited article: J.O Morales, K.R. Fathe, A. Brunaugh, S. Ferrati, S. Li, M. Montenegro-Nicolini, Z. Mousavikhamene, J.T. McConville, M.R. Prausnitz, H.D.C. Smyth, Challenges and Future Prospects for the Delivery of Biologics: Oral Mucosal, Pulmonary, and Transdermal Routes, *The AAPS Journal*, 2017, 1-17.

34. Guest Editor: Formulation and Delivery of Macromolecules, Special Edition: *AAPS PharmSciTech* 18 (2017).

35. Abstract Reviewer and Publication Coordinator for the Taylor & Francis Group and ExcipientFest 2017, Providence, RI.

36. Invited Article: I. Rossi, F. Sonvico, J. McConville, F. Rossi, E. Fröhlich, S. Zellnitz, A. Rossi, E. Del Favero, R Bettini, F. Buttini, Nebulized Coenzyme Q10 Nanosuspensions: A Versatile Approach for Pulmonary Antioxidant Therapy, *European Journal of Pharmaceutical Sciences*, 113 (2017), 159-170.

37. Session Judge: Academic and Industrial Posters, *Drug Delivery to the Lungs (DDL2017)*, Edinburgh, UK, December, 2017.

38. Session Judge: Pat Burnell Young Investigator Prize, *Drug Delivery to the Lungs (DDL2017)*, Edinburgh, UK, December, 2017.

39. Inducted as a member of the Tom L. Popejoy Society, *University of New Mexico*, 2018.

40. Elected: Member at Large Faculty Senate Health Sciences Center Council, *University of New Mexico*, July, 2018.

41. Session Judge: Academic and Industrial Posters, *Drug Delivery to the Lungs (DDL2018)*, Edinburgh, UK, December, 2018.

42. Session Judge: Academic and Industrial Posters, *Drug Delivery to the Lungs (DDL2018)*, Edinburgh, UK, December, 2018.

43. Keynote Speaker, *4th World Congress & Expo on Pharmaceutics and Drug Delivery Systems*, Milan, Italy, March, 2019.

44. Special Issue Guest Editor, Thin Film Technologies, *International Journal of Pharmaceutics*, November, 2019.

45. Session Judge: Academic and Industrial Posters, *Drug Delivery to the Lungs (DDL2019)*, Edinburgh, UK, December, 2019.

VIII. University Service and Committees Served

1. Chemical, Radiological, & Biohazard Safety Committee, University of Texas at Austin, College of Pharmacy, 2006-2008.

2. Pharmacokinetics Task Force, University of Texas at Austin, College of Pharmacy, 2006-2008.

3. Curriculum Committee, University of Texas at Austin, College of Pharmacy, 2009-2010.

4. Program Assessment Team, University of Texas at Austin, College of Pharmacy, 2009-2010.

5. Financial Aid Committee (Professional Student), University of Texas at Austin, College of Pharmacy, 2006-2012.

6. Admissions Committee, University of Texas at Austin, College of Pharmacy, 2008-2012.

7. Cultural Proficiency Committee, University of Texas at Austin, College of Pharmacy, 2008- 2012.

8. Pharmaceutics Division Graduate Advisor, University of Texas at Austin, College of Pharmacy, 2008-2012.

9. Promotion and Tenure Committee, Department of Pharmaceutical Sciences, University of New Mexico, 2012-present.

10. Web Re-Design Committee, College of Pharmacy, University of New Mexico, 2012-2013.

11. Staff Excellence Award Committee, College of Pharmacy, University of New Mexico, 2012-2013.

12. Faculty Development Committee, College of Pharmacy, University of New Mexico, 2012-Present. (2014-2015 -Vice Chair; 2015-2017 - Chair).

13. Institutional Animal Care and Use Committee (IACUC), Health Science Center, University of New Mexico, 2013-Present.

14. Accreditation Committee, College of Pharmacy, University of New Mexico, 2014-2016.

15. Graduate and Postdoctoral Affairs Committee, College of Pharmacy, University of New Mexico, 2015-2017.

16. Student Pharmacist Research Interest Group (SPRIG), College of Pharmacy, University of New Mexico, 2015 – 2017.

17. Pharmacy Year 1 Faculty Advisor, College of Pharmacy, University of New Mexico, Academic year 2017 - 2018.

18. Pharmacy Year 2 Faculty Advisor, College of Pharmacy, University of New Mexico, Academic year 2018 - 2019.

19. Pharmacy Year 3 Faculty Advisor, College of Pharmacy, University of New Mexico, Academic year 2019 - 2020.

20. Graduate Affairs Committee, College of Pharmacy, University of New Mexico, 2018 – 2019.

21. Office of Research and Compliance Academic Misconduct Special Investigation Committee, University of New Mexico, 2018 – 2019.

22. Research and Scholarship Committee, College of Pharmacy, University of New Mexico, 2018 – 2020.

23. Faculty Senate Health Sciences Center Council, University of New Mexico, 2018 – 2020.

24. Faculty Senate, University of New Mexico, 2020 – Present.

25. Health Science Library and Infomatics Center Advisory Council, Health Science Center, University of New Mexico, 2019 – Present.

26. UNM 2040 Steering Committee, University of New Mexico, 2021 – Present.

IX. Scientific Advisory Roles

1. Editorial Board Member of *Drug Development and Industrial Pharmacy*, 2007 – Present.

2. Editorial Advisory Board Member of *Inhalation*, 2007 – Present.

3. Prosolv® Advisory Board, JRS Pharma, Patterson, NY, 2009-2012.

4. Review Panel Member (*Ad-hoc*): National Institutes of Health, Center for Scientific Review, Nanotechnology Study Section, 2011.

5. Scientific Advisor for Respiratory Drug Delivery 2012, Phoenix, AZ, 2012.

6. American Association for the Advancement of Science, Research Competitiveness Program Review Committee (*Ad-Hoc*), New York Ave NW, Washington, DC, 2014.

7. Associate Editor of Special and Themed Issues for *Drug Development and Industrial Pharmacy*, 2015 – 2019.

8. Review Panel Member (*Ad-hoc*): National Institutes of Health, Center for Scientific Review, Special Emphasis Panel Study Section, 2017.

9. Scientific Advisor for the Aerosol Society, Drug Delivery to the Lungs (DDL), 2016 – Present.

10. Scientific Advisor for the International Pharmaceutical Excipients Council (IPEC) of the Americas, 2017 – 2019.

11. Editorial Board Member of the *Journal of Biopharmaceutics and Therapeutic Challenges*, 2017 – Present.

12. Review Panel Member (*Ad-hoc*): National Institutes of Health, Center for Scientific Review, Preclinical Services for HIV Therapeutics Special Emphasis Panel Study Section, 2020.

13. Associate Editor for *Drug Development and Industrial Pharmacy*, 2019 – Present.

14. Editorial Board Member of *Pharmaceutics*, 2020 – Present.

X. Teaching Experience

1. PHR352C (Lecture), Biopharmaceutics and Pharmacokinetics, Course Instructor, University of Texas at Austin, College of Pharmacy, 2007 - 2009.
2. PHR152P (Laboratory), Biopharmaceutics and Pharmacokinetics, Course Instructor, University of Texas at Austin, College of Pharmacy, 2007 - 2009.
3. PHR390S, Applied Pharmacokinetics, Course Coordinator, University of Texas at Austin, College of Pharmacy, 2007-2009.
4. PHR382R, Recent Advances in Pharmaceutics, Course Instructor, University of Texas at Austin, College of Pharmacy, 2007.
5. PHR380Q, Advanced Pharmaceutical Processing, Course Instructor, University of Texas at Austin, College of Pharmacy, 2008.
6. PHR380M, Drug Development, Course Instructor, University of Texas at Austin, College of Pharmacy, 2008.
7. PHR252C, Biopharmaceutics, Course Instructor, University of Texas at Austin, College of Pharmacy, 2009-2011.
8. PHR386Q, Preclinical and Clinical Drug Development, Course Instructor, University of Texas at Austin, College of Pharmacy, 2010-2012.
9. PHRM593, Pharmaceutical Sciences and Toxicology Seminar, Instructor of the Record (IOR), University of New Mexico, College of Pharmacy, 2014.
10. PHRM726, Biopharmaceutics and Pharmacokinetics, Course Instructor/Instructor of the Record (IOR), University of New Mexico, College of Pharmacy, 2012 – 2017.
11. PHRM702, Pharmaceutics II, Course Instructor, University of New Mexico, College of Pharmacy, 2013 – 2017.
12. PHRM598, Pharmaceutics & Drug Delivery Course Instructor/Instructor of the Record (IOR), University of New Mexico, College of Pharmacy, 2014.
13. PHRM701, Pharmaceutics I, Course Instructor, University of New Mexico, College of Pharmacy, 2016-2017.
14. PHRM802, Physical Pharmacy and Biopharmaceutics, Course Instructor/Instructor of the Record, University of New Mexico, College of Pharmacy, (IOR: 2017-Present).
15. PHRM824, Dosage Forms, Course Instructor, University of New Mexico, College of Pharmacy, 2017 – Present.

16. PHRM576, Molecular and Cellular Pharmacology, University of New Mexico, College of Pharmacy, 2017 – Present.

XI. Mentoring

Graduate Students and Postdoctoral Fellows

1. Yoen-Ju Son, Ph.D., Pharmaceutics Graduate Program, 2006-2010.
   Post-Doctoral fellow under supervision of Dr. Michael Hindle, Virginia Commonwealth University, 2011-2013.
2. Sumalee Thitinan, Ph.D., Pharmaceutics Graduate Program, University of Texas at Austin 2007-2011.Funded by a Thailand Government Pharmaceutical Organization Scholarship,
   Employer: Thailand Government Pharmaceutical Organization, 2011-present.
3. Thiago Carvalho Ph.D., Pharmaceutics Graduate Program, University of Texas at Austin, 2007-2011.
   Employer: Bristol-Myers Squibb, New Brunswick, New Jersey, 2011-present.
4. Matt Herpin, Pharmaceutics Graduate Program, University of Texas at Austin, 2011-2012.
5. Ping Du, Pharmaceutics Graduate Program, University of Texas at Austin, 2011-2012.
7. Ashkan Yazdi. Pharm.D./Ph.D Student Rotation, Pharmaceutics Graduate Program, University of Texas at Austin, 2011-2012.
8. Shih-Fan Jang, Ph.D., Pharmaceutics Graduate Program, University of Texas at Austin 2007-2013.
9. Javier Morales, Ph.D., Pharmaceutics Graduate Program, University of Texas at Austin 2008-2012. Funded by a Fulbright Organization Scholarship.
   Assistant Professor, Department of Pharmaceutical Sciences and Technology, University of Chile, 2013-present.
10. Simone Carvalho, Ph.D., Pharmaceutics Graduate Program, University of Texas at Austin 2009-2013.
11. Audrey Smith, Biomedical Sciences Graduate Program (BSGP) Student Rotation, University of New Mexico, Spring, 2013.
12. Dominique Perez, Biomedical Sciences Graduate Program (BSGP) Student Rotation, University of New Mexico, Spring, 2013.
13. Joseph Castillo, Biomedical Sciences Graduate Program (BSGP) Student Rotation, University of New Mexico, Fall, 2013.
14. Kai Berkenfeld Ph.D., Graduate Student, Department of Pharmaceutical Technology Graduate Program, University of Bonn, 2012-2019.

15. Anh-Le Dung, Nanoscience and Microsystems Engineering Graduate Program, University of New Mexico, 2013-2016.
16. Kristina Schönhoff M.S., Graduate Student, Department of Pharmaceutical Technology Graduate Program, University of Bonn, 2014-2016.
17. Sudha Ananthakrishnan M.S., Nanoscience and Microsystems Engineering Graduate Program, University of New Mexico, 2013-2016.
18. Elnaz Sadeghi M.S., Biomedical Engineering Graduate Program, University of New Mexico, 2016-2018.
19. Rikhav Gala, Ph.D., Research Scientist I, University of New Mexico, 2017-2018.

Pharm.D Students

1. Ashkan Yazdi. UT Pharm.D./Ph.D Student Rotation, 2008. (Honors Project)
2. Michelle Horng, UT Pharm.D. Student, 2008-2011.
3. Rajesh Peddaiahgari, UT Pharm.D. Student, 2009.
4. Yi Guo, UT Pharm.D. Student, 2009.
5. Tian Tian, UT Pharm.D./Ph.D Student Rotation, 2010/2011. (Honors Project)
6. Ashley Jewitt, UT B.S. Student, 2011-2012.
7. Nicole Wesley, UT Pharm.D. Student, Fall 2011.
8. Lessel Lamkin, UNM Pharm.D. Student, Spring 2012 – Spring 2014.
9. Colin Williams, UNM Pharm.D. Student, Spring 2012.
10. Michael Bernauer, UNM Pharm.D. Student, Spring 2013-Fall 2015.
11. Maria Gabriela Cabanilla, UNM Pharm.D. Student, Fall 2014 – Spring 2016.
12. Christina Clise, UNM Pharm.D. Student, Spring 2012 – Spring 2016.
13. Meghan Bass, UNM Pharm.D. Student, Spring 2016 – Spring 2017.
14. Jarrid Young, UNM Pharm.D. Student, Fall 2016 – Fall 2017.
15. Jason Solano, UNM Pharm.D. Student, Spring 2017-2018.
16. Joseph Dinallo, UNM Pharm.D. Student, Spring 2016-2017.
17. Anh Le, UNM Pharm.D. Student, Summer 2018 – Summer 2019.
18. Victoria Lopez, UNM Pharm.D. Student, Summer 2018 – Spring 2019.
19. Aaron Rodriguez, UNM Pharm.D. Student, Summer 2018 – Spring 2019.
20. Haya Albazzaz, UNM Pharm.D. Student, Spring 2020 – Present.
21. Erena Hovhannisyan, UNM Pharm.D. Student, Spring 2020 – Present.
22. Madison Robinette, UNM BSPS Student, Summer 2021 – Present.

Visiting Scholars

1. Simone Dietz, Pharmaceutics Intern from University of Bonn, Germany. Fall/Spring 2010/2011.
2. Christine Joseph, Pharmaceutics Intern from University of Bonn, Germany. Spring/Summer 2011.
3. Gero Joks, Pharmaceutics Intern from University of Bonn, Germany. Summer 2011.
4. Professor Alf Lamprecht, Visiting Professor from University of Bonn, Germany. Fall 2016.
5. Ian Morales, Pharmaceutics Intern from Department of Chemistry, University of Puerto Rico. Summer 2017.
6. Yousef Abugalyon, National Institute of Health (NIH) The University of Texas at El Paso BUILDing Scholars Program. Summer 2017.
7. William Mclain, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2017.
8. Adnan Hassan, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2017.
9. Liam Wade, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2018.
10. Haya Albazzaz, Volunteer Pre-Pharmacy Undergraduate Student, UNM, Fall 2018 – Summer 2019.
11. Hannah Avery, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2019.
12. Chrystabel Chinye, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2019.

Dissertation Committees Served

1. Justin Tolman, Ph.D., UT Pharmaceutics Graduate Program, 2009.
2. Piynauch Wonganan, Ph.D, UT Pharmaceutics Graduate Program, 2010.
3. Yoen-Ju Son, Ph.D., UT Pharmaceutics Graduate Program, 2010. (Chair)
4. Sumalee Thitinan, Ph.D., UT Pharmaceutics Graduate Program, 2011. (Chair)
5. Nicole Nelson, Ph.D, UT Pharmaceutics Graduate Program, 2011.
6. Martin Donovan, Ph.D, UT Pharmaceutics Graduate Program, 2011.
7. Shayna McGill, Ph.D, UT Pharmaceutics Graduate Program, 2011.
8. Nicole Nelson, Ph.D., UT Pharmaceutics Graduate Program, 2011.

9. Loti David King'ori, M.Sc., Pharmacy, Rhodes University, South Africa, 2011.
10. Thiago Carvalho Ph.D., UT Pharmaceutics Graduate Program, 2011. (Chair)
11. Helen Lirolla, Ph.D., UT Pharmaceutics Graduate Program, 2012.
12. Prinda Wanakule, Ph.D., UT BME Graduate Program, 2012.
13. Mehra Haghi, Ph.D., Pharmacy, University of Sydney, 2012.
14. Letty Rodriguez, Ph.D., UT Pharmaceutics Graduate Program, 2012.
15. Javier Morales, Ph.D., UT Pharmaceutics Graduate Program, 2012. (Chair)
16. Shih-Fan Jang, Ph.D., UT Pharmaceutics Graduate Program, 2013. (Chair)
17. Eileen Dawson, Ph.D., UT BME Graduate Program, 2013.
18. Amit Kumar, Ph.D., UT Pharmaceutics Graduate Program, 2013.
19. Simone Carvalho, Ph.D., UT Pharmaceutics Graduate Program, 2013. (Co-Chair)
20. Amber McBride, Ph.D., UNM NSME Graduate Program, 2014.
21. Kristina Schönhoff, M.S., Pharmaceutical Technology Graduate Program, University of Bonn, 2014. (Co-Chair)
22. Ashmita Ramanah, Pharmacy, Rhodes University, 2016.
23. Elnaz Sadeghi, M.S. UNM Biomedical Engineering Graduate Program, 2018. (Chair)
24. Kai Berkenfeld Ph.D., University of Bonn, Pharmaceutical Technology Graduate Program, 2019. (Co-Chair)
25. Sudha Ananthakrishnan M.S., UNM NSME Graduate Program, 2019. (Chair)

XII. Peer Reviewing

1. Drug Development and Industrial Pharmacy, Taylor & Francis Group, Abingdon, UK.
2. European Journal of Pharmaceutical Sciences, Elsevier, Amsterdam, Netherlands.
3. European Journal of Pharmaceutics and Biopharmaceutics, Elsevier, Amsterdam, Netherlands.
4. International Journal of Pharmaceutics, Elsevier, Amsterdam, Netherlands.
5. Journal of Controlled Release, Elsevier, Amsterdam, Netherlands.
6. Journal of Pharmaceutical Sciences, Elsevier, Amsterdam, Netherlands.
7. Pharmaceutical Research, Springer Nature, Basel, Switzerland.
8. Molecular Pharmaceutics, American Chemical Society, Washington, DC.

9. Ashley Publications Ltd., London, UK.
10. Drug Delivery, Taylor & Francis Group, Abingdon, UK.
11. Journal of Pharmacy and Pharmaceutical Sciences, Edmonton, Alberta, Canada.
12. Informa Healthcare USA, New York, NY
13. Pharmaceutical Press, London, UK
14. Journal of Pharmacy and Nutrition Science, Lifescience Global, Mississauga, Ontario, Canada.
15. Inhalation, CSC Publishing, St. Paul, MN.

XIII. Publications

1. J.T. McConville, N. Patel, N. Ditchburn, P. Woodcock, M.J. Tobyn, J.N. Staniforth, Use of a Novel Modified TSI for the Evaluation of Controlled-Release Aerosol Formulations, *Drug Development and Industrial Pharmacy*, 26(2000) 1191-1198.

2. J.T. McConville, A.C. Ross, A.R. Chambers, G. Smith, A.J. Florence, H.N.E. Stevens, The Effect of Wet Granulation on the Erosion Behavior of an HPMC–Lactose Tablet, Used as a Rate-Controlling Component in a Pulsatile Drug Delivery Capsule Formulation, *European Journal of Pharmaceutics and Biopharmaceutics*, 57(2004) 541-549.

3. J.T. McConville, A.C. Ross, A.J. Florence, H.N.E. Stevens, Erosion Characteristics of an Erodible Tablet Incorporated in a Time-Delayed Capsule Device, *Drug Development and Industrial Pharmacy*, 31(2005) 79-89.

4. J.T. McConville, Recent Trends in Oral Drug Delivery, *The Drug Delivery Companies Report*, PharmaVentures, Oxford, UK, Autumn/Winter (2005) 24-27.

5. J.T. McConville, T.C. Carvalho, A.N. Iberg, R.L. Talbert, D.S. Burgess, J.I. Peters, K.P. Johnston, R.O. Williams III, Design and Evaluation of a Restraint-Free Small Animal Inhalation Dosing Chamber, *Drug Development and Industrial Pharmacy*, 31(2005) 35-42.

6. B.J. Hoeben, D.S. Burgess, J.T. McConville, L.K. Najvar, R.L. Talbert, J.I. Peters, N.P. Wiederhold, B.L. Frei, J.R. Graybill, R. Bocanegra, K.A. Overhoff, P. Sinswat, K.P. Johnston and R.O. Williams III, *In Vivo* Efficacy of Aerosolized Nanostructured Itraconazole Formulations for the Prevention of Invasive Pulmonary Aspergillosis, *Antimicrobial Agents and Chemotherapy*, 50(2006) 1552-1554.

7. J.M. Vaughn, J.T. McConville, X. Gao, M.T. Crisp, K.P. Johnston, R.O. Williams III, Supersaturation Produces High Bioavailability of Amorphous Danazol Particles Formed by Evaporative Precipitation into Aqueous Solution and Spray Freezing into Liquid Technologies, *Drug Development and Industrial Pharmacy*, 32(2006) 559-567.

8. J.T. McConville, K.A. Overhoff, P. Sinswat, J.M. Vaughn, B.L. Frei, D.S. Burgess, R.L. Talbert, J.I. Peters, K.P. Johnston, R.O. Williams III, Targeted High Lung Concentrations of Itraconazole Using Nebulized Dispersions in a Murine Model, *Pharmaceutical Research*, 23(2006) 901-911.

9. J.M. Vaughn, J.T. McConville, D.S. Burgess, J.I. Peters, K.P. Johnston, R.L. Talbert, R.O. Williams III, Single Dose and Multiple Dose Studies of Aerosolized Itraconazole Nanoparticles, *European Journal of Pharmaceutics and Biopharmaceutics*, 63(2006) 95-102.

10. T. Purvis, J.M. Vaughn, T.L. Rogers, X. Chen, K.A. Overhoff, P. Sinswat, J. Hu, J.T. McConville, K.P. Johnston, R.O. Williams III, Cryogenic liquids, Nanoparticles, and Microencapsulation, *International Journal of Pharmaceutics*, 324(2006) 43-50.

11. J.T. McConville, N.P. Wiederhold, Antifungal Prophylaxis to the Lung Using Itraconazole, *Inhalation*, 1(2007) 6-9.

12. J.T. McConville, Targeted Lung Delivery of Antifungals: Preclinical Studies Using Itraconazole Nanoparticles, *RDD Europe 2007*, 1(2007) 43-50.

13. D.A. Miller, J.T. McConville, W. Yang, R.O. Williams III, J.W. McGinity, Hot-Melt Extrusion for Enhanced Delivery of Drug Particles, *Journal of Pharmaceutical Sciences*, 96(2007) 361-76.

14. J.M. Vaughn, N.P. Wiederhold, Jason T. McConville, J.J. Coalson, R.L. Talbert, D.S. Burgess, K.P. Johnston, R.O. Williams III, Murine Airway Histology and Alveolar Macrophage Uptake of Inhaled Amorphous Itraconazole, *International Journal of Pharmaceutics*, 338(2007) 219-224.

15. C.A. Alvarez, N.P. Wiederhold, J.T. McConville, J.I. Peters, L.K. Najvar, J.R. Graybill, J.J. Coalson, R.L. Talbert, D.S. Burgess, R. Bocanegra, K.P. Johnston, R.O. Williams III, Aerosolized Nanostructured Itraconazole as Prophylaxis Against Invasive Pulmonary Aspergillosis, *Journal of Infection*, 55(2007) 68-74.

16. M. T. Carvajal, D. Cipolla, M. Copley, J.T. McConville, Highlights from RDD 2008: *Inhalation* Reports on Some of the Most Interesting Research Presented at the Most Recent Respiratory Drug Delivery Meeting, *Inhalation*, 2:3(2008) 18-20.

17. K.A. Overhoff, J.T. McConville, W. Yang, K.P. Johnston, J.I. Peters, R.O. Williams, Effect of Stabilizer on the Maximum Degree and Extent of Supersaturation and Oral Absorption of Tacrolimus Made by Ultra-Rapid Freezing, *Pharmaceutical Research*, 25(2008) 167-175.

18. W. Yang, J. Tam, D.A. Miller, J. Zhou, J.T. McConville, K.P. Johnston, R.O. Williams III, High Bioavailability from Nebulized Itraconazole Nanoparticle Dispersions with Biocompatible Stabilizers, Special Edition: Pharmaceutical Nanotechnology, *International Journal of Pharmaceutics*, 361(2008) 177–188.

19. J. Tam, J.T. McConville, R.O. Williams III, K.P. Johnston, Amorphous Cyclosporin-A Nanodispersions for Enhanced Pulmonary Deposition and Dissolution, *Journal of Pharmaceutical Sciences*, 97(2008) 4915-4933.

20. P. Sinswat, K.A. Overhoff, J.T. McConville, K.P. Johnston, Robert O. Williams III, Nebulization of Nanoparticulate Amorphous or Crystalline Tacrolimus – Single-Dose Pharmacokinetics Study in Mice, *European Journal of Pharmaceutics and Biopharmaceutics*, 69(2008) 1057-1066.

21. Y-J. Son, J.T. McConville, Advancements in Dry Powder Delivery to the Lung, Special Edition: Innovative Inhalation Technologies, *Drug Development and Industrial Pharmacy*, 34(2008) 948-959.

22. A.B. Watts, J.T. McConville, R.O. Williams III, Current Therapies and Technological Advances in Aqueous Aerosol Drug Delivery, Special Edition: Innovative Inhalation Technologies, *Drug Development and Industrial Pharmacy*, 34(2008) 913-922.

23. S. Thitinan, J.T. McConville, Interferon Alpha Delivery Systems for the Treatment of Hepatitis C, *International Journal of Pharmaceutics*. 369(2009) 121-135.

24. J.T. McConville, S.A. Kucera, T.C. Carvalho, E.M. Hurley, Ethyl Lactate as a Pharmaceutical-Grade Excipient and Development of a Sensitive Peroxide Assay, *Pharmaceutical Technology*, 33(2009) 74-84.

25. Y-J Son, J.T. McConville, Dissolution Testing for Inhalation Formulations, *Inhalation*, 2:6(2009) 8-11.

26. J.T. McConville, L. Hodges, T. Jones, J.P. Band, B. O'Mahony, B. Lindsay, A.C. Ross, A.J. Florence, A.J. Stanley, M.J. Humphrey, C.G. Wilson, H.N.E. Stevens, A Pharmacoscintigraphic Study of Three Time-Delayed Capsule Formulations in Healthy Male Volunteers, *Journal of Pharmaceutical Sciences*, 98(2009) 4251-4263.

27. J.A. Tolman, N.A. Nelson, Y-Ju Son, S. Bosselmann, N.P. Wiederhold, J.I. Peters, J.T. McConville, R.O. Williams III, Characterization and Pharmacokinetic Analysis of Aerosolized Aqueous Voriconazole Solution, *European Journal of Pharmaceutics and Biopharmaceutics* 72(2009) 199-205.

28. J.A. Tolman, N.P. Wiederhold, J.T. McConville, L.K. Najvar, R. Bocanegra, J.I. Peters, J.J. Coalson, J.R. Graybill, T.F. Patterson, R.O. Williams III, Inhaled Voriconazole for the Prevention of Invasive Pulmonary Aspergillosis, *Antimicrobial Agents and Chemotherapy*, 53(2009) 2613-2615.

29. Y-J. Son, J.T. McConville, A Standardized Dissolution Test Method for Inhaled Pharmaceutical Formulations, *International Journal of Pharmaceutics*, 382(2009) 15-22.

30. J.O. Morales, M. Horng, A.M. Gregg, J.T. McConville, Development of Orally-Disintegrating Tablets using Starch and Fructose, *Pharmaceutical Technology*, 34(2010), 92-99.

31. Y-J. Son, M. Horng, M. Copley, J.T. McConville, Optimization of an *In Vitro* Dissolution Test Method for Inhalation Formulations, *Dissolution Technologies*, 17(2010), 6-13.

32. M. Copley, Y-J. Son, J. McConville, Dissolution Testing for Inhaled Drugs, *Pharmaceutical Technology Europe*, 22(2010), 37-38, 40-43.

33. T.C. Carvalho, S.R. Carvalho, J.T. McConville, Formulations for Pulmonary Administration of Anticancer Agents to Treat Lung Malignancies, *Journal of Aerosol Medicine and Pulmonary Drug Delivery*, 24(2011), 61-80.

34. J.O. Morales, J.T. McConville, Manufacture and Characterization of Mucoadhesive Buccal Films, *European Journal of Pharmaceutics and Biopharmaceutics*, 77(2011), 187-199.

35. Y-J. Son, J.T. McConville, A New Respirable Form of Rifampicin, *European Journal of Pharmaceutics and Biopharmaceutics*, 78 (2011), 366-376.

36. T. Carvalho, M. Horng, J.T. McConville, Application of a Pull on a Disk Method to Measure Surface Tension of Liquids, *AAPSPharmSciTech*, 13 (2012), 305-312.

37. Y-J. Son, J.T. McConville, A Prospective Dissolution Test Design: Controlling the Important Variables, *Respiratory Drug Delivery 2012*, 1(2012) 177-184.

38. S. Thitinan, J.T. McConville, Development of a Gastroretentive Pulsatile Drug Delivery Platform, *Journal of Pharmacy and Pharmacology*, 64 (2012), 505-516.

39. Y-J. Son, J.T. McConville, Preparation of Sustained Release Rifampicin Microparticles for Inhalation, Special Edition: *Journal of Pharmacy and Pharmacology*, 64 (2012), 1291-1302.

40. A.K. Yazdi, J.O. Morales, S.R. Marek, F. Thielmann, D. Burnett, J. Heng, J.T. McConville, Dissolution Rate Comparison of Micronized and Spray-Dried Budesonide, *Respiratory Drug Delivery 2012*, 3 (2012), 855-858.

41. S-F Jang, B.A. Goins, W.T. Phillips, C. Santoyo, A.R-Ficht, J.T. McConville, Size Discrimination in Rodent Gastric Emptying, *Biopharmaceutics & Drug Disposition*, 34 (2013), 107–124.

42. J.O. Morales, R. Su, J.T. McConville, The Influence of Recrystallized Caffeine on Water-Swellable Polymethacrylate Mucoadhesive Buccal Films, *AAPS PharmSciTech*, 14 (2013) 475-484.

43. J.O. Morales, G.R. Joks, A. Lamprecht, J.T. McConville A design of experiments to optimize a new manufacturing process for high activity protein-containing submicron particles, *Drug Development and Industrial Pharmacy*, 39 (2013), 1793-1801.

44. J.O. Morales, A.C. Ross, R. Su, J.T. McConville. Protein-coated nanoparticles embedded in films for buccal delivery. *Journal of Pharmacy and Pharmacology*, 65 (2013), 827–838.

45. T.C. Carvalho, J.P. McCook, N.R. Narain, J.T. McConville, Development and Characterization of Phospholipid-Stabilized Submicron Aqueous Dispersions of Coenzyme Q_{10} Presenting Continuous Vibrating-Mesh Nebulization Performance, *Journal of Liposome Research*, 23 (2013), 276-290.

46. J. Hautmann, S.E. Godoy, P. Marshik, R. Chand, J. McConville, S. Krishna, S. Krishna, P. Muttil, Effect of Time Between Actuation on the Dose Variability for Three Metered Dose Inhalers, *Respiratory Drug Delivery 2013*, 2 (2013), 429-434.

47. J.O. Morales, J.T. McConville, Novel Strategies for the Buccal Delivery of Macromolecules, *Drug Development and Industrial Pharmacy*, 40 (2014), 579–590.

48. J.O. Morales, S. Huang, R.O. Williams III, J.T. McConville, Films loaded with Insulin-coated nanoparticles (ICNP) as potential platforms for peptide buccal delivery, *Colloids and Surfaces B: Biointerfaces*, 122 (2014), 38–45.

49. M.E. Ali, J.T. McConville, A. Lamprecht, Pulmonary Delivery of Anti-Inflammatory Agents, *Expert Opinion on Drug Delivery*, 12 (2015), 929-945.

50. K. Berkenfeld, A. Lamprecht, J.T. McConville, Devices for Dry Powder Drug Delivery to the Lung, Special Edition: Advances in Formulation and Device Technologies for Pulmonary Drug Delivery, *AAPSPharmSci Tech*, 16 (2015), 479-490.

51. J.E. Hasted P. Bäckman, A.R. Clark, W. Doub, A. Hickey, G. Hochhaus, P.J. Kuehl, C-M. Lehr, P. Mauser, J. McConville, R. Niven, M. Sakagimi and J.G. Weers, Scope and relevance of a pulmonary biopharmaceutical classification system AAPS/FDA/USP Workshop March 16-17th, 2015 in Baltimore, MD, *AAPS Open*, 2 (2016), 1-20.

52. T.C. Carvalho, J.T. McConville, The Function and Performance of Aqueous Aerosol Devices for Inhalation Therapy, *Journal of Pharmacy and Pharmacology*, 68 (2016), 68(5), 556-578.

53. T.C. Carvalho, J.P. McCook, N.R. Narain, J.T. McConville, Development of Aqueous Dispersions of Coenzyme Q10 for Pulmonary Delivery and the Dynamics of Active Vibrating-Mesh Aerosolization, Special Issue: Staniforth Festschrift, *International Journal of Pharmaceutics*, 514 (2016), 407-419.

54. J.O Morales, K.R. Fathe, A. Brunaugh, S. Ferrati, S. Li, M. Montenegro-Nicolini, Z. Mousavikhamene, J.T. McConville, M.R. Prausnitz, H.D.C. Smyth, Challenges and Future Prospects for the Delivery of Biologics: Oral Mucosal, Pulmonary, and Transdermal Routes, *The AAPS Journal*, (2017), 1-17.

55. I. Rossi, F. Sonvico, J. McConville, F. Rossi, E. Fröhlich, S. Zellnitz, A. Rossi, E. Del Favero, R Bettini, F. Buttini, Nebulized Coenzyme Q10 Nanosuspensions: A Versatile Approach for Pulmonary Antioxidant Therapy, *European Journal of Pharmaceutical Sciences*, 113 (2018), 159-170.

56. K. Berkenfeld, M. Bernauer, J.T. McConville, A. Lamprecht, Investigating Cascade Impactor Performance using a Modified 3D Printed Induction Port, *International Journal of Pharmaceutics*, 535 (2018), 402-409.

57. K. Berkenfeld, K. Hauschild, J.T. McConville, A. Lamprecht, Cascade Impactor Performance of Commercial pMDI Formulations using Modified Induction Ports, *Molecular Pharmaceutics*, 17 (2020), 1491–1501.

58. K. Berkenfeld, J.T. McConville, A. Lamprecht, Inhalable Dry Powders of Rifampicin Highlighting Potential and Drawbacks in Formulation Development for Experimental Tuberculosis Aerosol Therapy, *Expert Opinion on Drug Delivery*, 17 (2020), 305-322.

59. K. Berkenfeld, J.T. McConville, A. Lamprecht, Inhalable Formulations of Rifampicin by Spray Drying of Supersaturated Aqueous Solutions, *European Journal of Pharmaceutics and Biopharmaceutics*, 153 (2020), 14-22.

60. K. Berkenfeld, J.T. McConville, A. Lamprecht, (Solvato-) Polymorphism of Spray Dried Formulations of Rifampicin for Pulmonary Drug Delivery, *International Journal of Pharmaceutics*, 590 (2020), 119932.

61. R.T. Sterk, A. Battle, H. Albazaz, M.A. Ozbun, J.T. McConville, The Effect of Thermal Gelation Agents on Aerosolization Properties of Viscous Liquids – In Preparation.

XIV. Published Abstracts

1. An *In Vitro* Method for Evaluation of Dry Powder Inhaler Formulations using a Novel Modified Twin Stage Impinger, Annual Meeting of the American Association of Pharmaceutical Scientists, Boston, MA, November, 1997.
2. A Novel *Ex Vivo* Method for Determining Diffusion Rates of Dry Powder Inhaler Formulations using an Isolated Perfused Guinea Pig Lung Model, Annual Meeting of the American Association of Pharmaceutical Scientists, Boston, MA, November, 1997.
3. The Comparison of Two Delivery Techniques for Dosing an Isolated Perfused Guinea Pig Lung (IPGPL), Annual Meeting of the American Association of Pharmaceutical Scientists, San Francisco, CA, November, 1998
4. An *In Vitro* Method for Evaluation of Lung Deposition and Drug Diffusion from Dry Powder Formulations using a Modified Twin Stage Impinger, Annual Meeting of the American Association of Pharmaceutical Scientists, San Francisco, CA, November, 1998.
5. Preclinical Evaluation of an Isotretinoin (iso) Powder Formulation for Aerosol Administration in Lung Cancer Chemoprevention, 90th American Association of Cancer Research, Philadelphia, PA, April, 1999.
6. Effect of Process Variables on the Time-delayed Release from a Capsule Based Delivery Device, 23rd Joint Research Seminar, Dublin, Ireland, June, 2000.
7. Effect of Process Variables on Drug Release from a Time-Delayed Capsule Delivery System, 137th British Pharmaceutical Conference, Birmingham, United Kingdom, September, 2000.
8. Processing Induced Variability of Time-delayed Delivery from a Pulsatile Capsule Device, Annual Meeting of the American Association of Pharmaceutical Scientists, Indianapolis, IN, October, 2000.
9. Microwave Dielectric Analysis of Wet Granulations for Erodible HPMC Tablets, 138th British Pharmaceutical Conference, Glasgow, United Kingdom, September, 2001.
10. The use of Microwave Analysis to Describe the Effect of a Wet Granulation Processing Technique, Annual Meeting of the American Association of Pharmaceutical Scientists, Denver, CO, October, 2001.
11. Gamma Scintigraphic Visualisation of Drug Release from a Time-Delayed Capsule, 6th US-Japan Drug Delivery Symposium, Honolulu, HI, November, 2001.
12. Gamma Scintigraphic Investigation of Drug Release from a Time-Delayed Capsule, 29th International Symposium on Controlled Release of Bioactive Materials, Seoul, Korea, June, 2002.
13. Preparation of Water-impermeable Capsule Bodies for a Pulsatile Drug Delivery System, 139th British Pharmaceutical Conference, Manchester, United Kingdom, September, 2002.
14. Time Delayed Delivery of Theophylline, 139th British Pharmaceutical Conference, Manchester, United Kingdom, September, 2002.

15. The Suitability of a Capsule Component for use with a Pulsed Release Drug Delivery Device, Annual Meeting of the American Association of Pharmaceutical Scientists, Toronto, Canada, November, 2002.
16. Gastrointestinal Transit and Release of Time-Delayed Delivery Capsules, Annual Meeting of the American Association of Pharmaceutical Scientists, Toronto, Canada, November, 2002.
17. A Study to Investigate the effects of Food Administration Post-Gastric Emptying on a Time-delayed Formulation in Healthy Volunteers using Gamma Scintigraphy, 30th International Symposium on Controlled Release of Bioactive Materials, Glasgow, United Kingdom, June, 2003.
18. Physiochemical Properties of Itraconazole Produced by Spray-Freezing into Liquid Process, 1st European Federation for Pharmaceutical Sciences Conference on Optimizing Drug Delivery and Formulation: New Challenges in Drug Delivery, Versailles, France, September, 2003.
19. Controlling Particle Characteristics of Itraconazole Powders Produced by Spray-freezing into Liquid - Organic Solution Versus Emulsion Liquid Feed Solutions, Annual Meeting of the American Association of Pharmaceutical Scientists, Salt Lake City, UT, October, 2003.
20. Nebulization of a Suspension Containing Itraconazole Prepared by Evaporative Precipitation into Aqueous Solution, Annual Meeting of the American Association of Pharmaceutical Scientists, Salt Lake City, UT, October, 2003.
21. Spray Freezing into Liquid of Itraconazole for Pulmonary Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, Salt Lake City, UT, October, 2003.
22. Enhanced Solubility and Dissolution of Itraconazole Prepared by the Spray Freezing into Liquid Technique, 31st International Symposium on Controlled Release of Bioactive Materials, Honolulu, HI, June, 2004.
23. The Use of Antioxidants to Stabilize Ethyl Lactate, Annual Meeting of the American Association of Pharmaceutical Scientists, Baltimore, MD, November, 2004.
24. Design of a Restraint-Free Small Animal Dosing Chamber for Inhalation and Investigation of Drug Distribution Within the Chamber, Annual Meeting of the American Association of Pharmaceutical Scientists, Baltimore, MD, November, 2004.
25. Miscibility of Hydrophilic Polymers and Surfactants with Polyethylene Oxide in Hot-melt Extruded Tablets Containing Poorly Water Soluble Drug, Annual Meeting of the American Association of Pharmaceutical Scientists, Baltimore, MD, November, 2004.
26. Delivery of Poorly Water Soluble Drugs using Nebulization, 15th Drug Delivery to the Lungs Conference, London, United Kingdom, December, 2004.
27. Improved Dissolution Rate and Bioavailability through the Formation of a Highly Miscible Binary Mixture, 32nd International Symposium on Controlled Release of Bioactive Materials, Miami, FL, June, 2004.
28. Delivery of Nebulized Itraconazole Nanoparticles in the Murine Model, Respiratory Drug Delivery Europe 2005, Paris, France, May, 2005.

29. Particle Engineering for Rapid Dissolution Rates of Poorly Water Soluble Drugs, American Institute of Chemical Engineers (AIChE) Annual Meeting, Cincinnati, OH, October, 2005
30. Investigation of Dissolution Properties of Microcrystalline or Stabilized Amorphous Particles of Itraconazole in Melt Extruded Solid Dispersions, Joint Symposium on the Future Prospects of Pharmaceutical Sciences, Hoshi University, Tokyo, Japan, October, 2005.
31. Characterization of Nebulized Itraconazole Nanoparticles and Delivery to the Murine Lung, Annual Meeting of the American Association of Pharmaceutical Scientists, Nashville, TN, November, 2005.
32. Treatment of Acute Pulmonary Aspergillosis with Nebulized Itraconazole in the Murine Model, Annual Meeting of the American Association of Pharmaceutical Scientists, Nashville, TN, November, 2005.
33. Improved Danazol Supersaturation and Oral Bioavailability via Formulation into an Amorphous Solid Solution, Annual Meeting of the American Association of Pharmaceutical Scientists, Nashville, TN, November, 2005.
34. Investigation of Dissolution Properties of Microcrystalline or Stabilized Amorphous Particles of Itraconazole in Melt Extruded Solid Dispersions, Annual Meeting of the American Association of Pharmaceutical Scientists, Nashville, TN, November, 2005.
35. Treatment of Pulmonary Aspergillosis using Nebulized Itraconazole Nanoparticles prepared using Particle Engineering Technologies, 16th Drug Delivery to the Lung Conference, London, United Kingdom, December, 2005.
36. *In Vivo* Efficacy of Aerosolized Nano-structured Itraconazole (ITZ) Formulations for the Prevention of Invasive Pulmonary Aspergillosis (IPA), 45th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, DC, December 2005 (originally scheduled for New Orleans, September, 2005).
37. Single Dose Variability and Multi-Dose Studies of Nebulized Itraconazole in a Murine Model, Respiratory Drug Delivery (RDD X) Conference, Boca Raton, FL, April, 2006.
38. Murine Airway Histology and Alveolar Macrophage Uptake of Inhaled Amorphous Itraconazole (Itra), American Thoracic Society International Conference, San Diego, CA, May, 2006.
39. Particle Engineering and Formulation for Enhanced Bioavailability of Poorly Water Soluble Drugs, Particles 2006 Conference, Orlando, FL, May, 2006.
40. Sustained Lung Concentrations of Itraconazole using Nebulized Dispersions in a Murine Model, 32nd International Symposium on Controlled Release of Bioactive Materials, Vienna, Austria, July, 2006.
41. Aerosolized Itraconazole (ITZ) as Prophylaxis against Invasive Pulmonary Aspergillosis (IPA) due to *Aspergillus fumigatus*, American College of Clinical Pharmacy Annual Meeting, St. Louis, MS, October, 2006.
42. *In-vitro* and *In-vivo* Comparison of Melt Extruded Particulate Dispersions of PVP and HPMC-Stabilized Nano-Structured Amorphous Itraconazole Particles, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, October, 2006.

43. Antisolvent Precipitation of Cyclosporin A Nanoparticles for Enhanced Pulmonary Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, October, 2006.
44. Immunological Response and Alveolar Macrophage Uptake of Inhaled Amorphous ITZ, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, October, 2006.
45. *In Vitro* and *In Vivo* Validation of a High-Concentration Pre-Clinical Rodent Dosing Apparatus for Inhalation, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, October, 2006.
46. A Novel *In Vitro* Pulmonary Dissolution Testing Method for Controlled Release Inhalation Formulations, 34th International Symposium on Controlled Release of Bioactive Materials, Long Beach, CA, July, 2007.
47. The Swelling Properties of Walocel-HM (Hypromellose) in 100% Ethanol, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2007.
48. A Novel *In Vitro* Dissolution Testing Method for Inhalation Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2007.
49. *In Vitro* Determination of Gastric Mucoadhesion for Hypromellose Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2007.
50. Development of a Standardized *In Vitro* Pulmonary Dissolution Testing Method, 6th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Barcelona, Spain, April 2008.
51. Development of a Standardized Dissolution Test for Inhalable Formulations, Respiratory Drug Delivery (RDD XI) Conference, Scottsdale, AZ, May, 2008.
52. *In Vitro* Determination of Gastrointestinal Mucoadhesion Formulations, 35th International Symposium on Controlled Release of Bioactive Materials, New York, NY, July, 2008.
53. Aerosolized Voriconazole (VRC) as Prophylaxis against Invasive Pulmonary Aspergillosis (IPA) due to *Aspergillus fumigatus*, 48th Interscience Conference on Antimicrobial Agents and Chemotherapy/Infectious Diseases Society of America 46th Annual Meeting, Washington, DC, October, 2008.
54. Preliminary Studies for Rapidly Disintegrating Mini-Tablets for Enteric Coated Oral Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
55. Gender and Race-Based Disparities in the Proportion of Hepatitis C Patients that are Co-Infected with HIV/AIDS in The 1996-2005 US National Hospital Discharge Survey, Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
56. Low Concentration Range Determination of API 31510 using High Performance Liquid Chromatography (HPLC), Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
57. Major Sites of Pulmonary Malignancy and Associated Health Outcomes for Lung Cancer Patients in the 1996-2005 National Hospital Discharge Survey (NHDS),

Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.

58. Improvements of an *In Vitro* Dissolution Test Method For Dry Powder Inhalation Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
59. Aerosol Characterization and Single-Dose Pharmacokinetic Analysis of Nebulized Voriconazole Solution, Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
60. Investigation of Nebulized Dose and Inhaled Dose of Itraconazole Dispersions in a Nose-Only Rodent Dosing Chamber, Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
61. Characterization of Saccharide Derived Fast Disintegrating Tablets, ExcipientFest 2009, San Juan, PR, May, 2009.
62. Manufacture and Characterization of Natural Polymer Based Films as Buccal Delivery Systems, ExcipientFest 2009, San Juan, PR, May, 2009.
63. Development of Fast Disintegrating Tablets using Starch and Starch Derivatives, 36th International Symposium on Controlled Release of Bioactive Materials, Copenhagen, Denmark, July, 2009.
64. An Investigation of Natural Based Films Suitable for Buccal Delivery, 36th International Symposium on Controlled Release of Bioactive Materials, Copenhagen, Denmark, July, 2009.
65. Effect of Oral Candidiasis Co-Infection in HIV/AIDS and Hepatitis C Patients Admitted to Hospitals in The United States, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
66. Effect of Cooling Rate on the Particle Size of API31510 Emulsions, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
67. Investigation of nebulized itraconazole dispersions: *in-vitro-in-vivo* comparison of dose administered to mice in a nose-only dosing apparatus, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
68. Nanostructured Tacrolimus Produced by Ultra-Rapid Freezing for Dry Powder Inhalation, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
69. Development and Evaluation of a Manufacturing Process for Xanthan Gum-Based Films, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
70. Optimization of an In Vitro Dissolution Test Method for Inhalation Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
71. Low Density Chitosan-Based Particles Prepared by Spray Drying as a Pulmonary Drug Delivery Vehicle, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.

72. Particle Manufacture for Targeted Oral Delivery in a Rodent Model, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
73. Development of Submicron Aqueous Formulations of API31510, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
74. Manufacture and characterization of Fast Disintegrating Tablets, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
75. Optimization of an In Vitro Dissolution Test Method for Inhalation Formulations, Proceeding of the Drug Delivery to the Lungs Conference (DDL20), Edinburgh, UK, December 2010.
76. The Use of Silicified Microcrystalline Cellulose and Fructose in the Development of Orally Disintegrating Tablets, 37th International Symposium on Controlled Release of Bioactive Materials, Portland, OR, July, 2010.
77. Rapidly Disintegrating Tablets for Targeted Oral Delivery, 37th International Symposium on Controlled Release of Bioactive Materials, Portland, OR, July, 2010.
78. Assessment of Student Performance in Biopharmaceutics using the TurningPoint Audience Response System, Proceedings of AACP Annual Meeting and Seminars, Seattle, WA, 2010.
79. Development and Characterization of Films for Buccal Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
80. Time Dependent Aerosolization Stability of Vibrating-Mesh Nebulizers with Submicron Lecithin Aqueous Dispersions of API31510, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
81. Nebulization Performance of Submicron Aqueous Dispersions of API 31510 prepared using High Pressure Homogenization, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
82. Measurement of Surface Tension of Liquids using Texture Analyzer, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
83. Manufacture of BSA Microcrystals by a Co-Precipitation Method, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
84. Stabilized Buoyancy and Optimal Loading Capacity of a Floating Gastric Device, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
85. Size Exclusion and Gastric Emptying in Rodent Models, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
86. Fighting Dysphagia with Orally Disintegrating Tablets, 8th International Conference on Functional Foods for Chronic Diseases: Science and Practice, Las Vegas, NV, March 2011.

87. Time Dependent Aerosolization Stability of a Vibrating-Mesh Nebulizer using API31510, Respiratory Drug Delivery Europe 2011, Berlin, Germany, May, 2011.
88. The Influence of Physicochemical Properties of Aqueous Dispersions on Active Vibrating-Mesh Nebulization, 18th Congress of International Society for Aerosols in Medicine, Rotterdam, Netherlands, June, 2011.
89. Orally Disintegrating Dietary Supplement Tablets, Institute of Food Technology Annual Meeting, New Orleans, LA, June, 2011.
90. A Gastric Retention Modeling Study of Floating Devices, 38th International Symposium on Controlled Release of Bioactive Materials, National Harbor, MD, July, 2011.
91. Impact of Drying Conditions on the Physicochemical and Aerodynamic Properties of Rifampicin Dihydrate (RFDH) Microcrystals, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington DC, October, 2011.
92. BSA Microcrystals by a Co-Precipitation Method: The Effect of Solvent Type and Presence of Surfactant, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington DC, October, 2011.
93. The Influence of Particles on Physical Properties of Films, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington DC, October, 2011.
94. *In Vitro* Evaluation of Adhesion Properties of Mucoadhesive Pellets Using Artificial Agar/Mucin Gel, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington DC, October, 2011.
95. The Influence of Physicochemical Properties of Aqueous Dispersions on Active Vibrating-Mesh Nebulization, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington DC, October, 2011.
96. Dissolution Rate Comparison of Micronized and Spray-Dried Budesonide, Respiratory Drug Delivery 2012, Phoenix, AZ, May, 2012.
97. A Novel Method for the Manufacture of Protein-Coated Nanoparticles, 39th International Symposium on Controlled Release of Bioactive Materials, Quebec City, Canada, July, 2012.
98. Dissolvable Strip for Treatment of Oral Thermal Burns, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
99. The Effect of pH on Protein-coated Submicron Particles Obtained by Antisolvent Co-precipitation, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
100. Manufacture and Characterization of Films for Buccal Delivery of Protein-coated Submicron Particles, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
101. Influence of Particulate API in Eudragit® RS and RL Films for Buccal Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
102. Controlled Release Properties of Cellulose Processed by Rapid Freezing Technology, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.

103. Prediction of *In Vitro* Aerosolization Profiles Based on Rheological Behaviors for Aqueous Dispersions of API 31510, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
104. Acoustic Levitation to Simulate Rifampicin Spray Drying Kinetics, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
105. Multiple Dose Platforms for Once-Daily Administration of Ciprofloxacin or Verapamil, 3rd International Conference and Exhibition on Pharmaceutics & Novel Drug Delivery Systems, Northbrook, IL, April, 2013.
106. Effect of Time Between Actuation on the Dose Variability for Three Metered Dose Inhalers, Respiratory Drug Delivery Europe 2013, Berlin, Germany, May, 2013.
107. Controlled Release Mucoadhesive Films Containing Nanoparticles of Lysozyme, 40th International Symposium on Controlled Release of Bioactive Materials, Honolulu, HI, July, 2013.
108. Determination of Thermodynamic Characteristics of A Rifampicin Solvate Recrystallized from Ethanol, 31st Annual Meeting of the Mountain West Society of the Society of Toxicology, Albuquerque, NM, September, 2013.
109. Bioadhesive Films Containing Nanoparticles of Lysozyme, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, November, 2013.
110. Development of Films of Insulin-coated Nanoparticles for Use in Buccal Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, November, 2013.
111. Gastroretentive Capsules for Once-daily Administration of Ciprofloxacin or Verapamil, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, November, 2013.
112. Preformulation Development Studies of Respirable Rifampicin Particles through Crystal Modification, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, November, 2013.
113. Inhaled Therapeutics for Lung Cancer, Drug Delivery to the Lungs Conference (DDL24), Edinburgh, UK, December, 2013.
114. Antisolvent Co-Precipitation Synthesis of D,L-Valine/Lysozyme, ExcipientFest 2014, Raleigh, NC, April, 2014.
115. Antisolvent Co-precipitation Synthesis of D,L-Valine/Lysozyme (Encore Presentation), Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2014.
116. Core Forming Antisolvent Co-precipitation of Protein Loaded Crystals, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2014.
117. Investigating of Protein-Coated Nanoparticles for Controlled Release Films, 42nd International Symposium on Controlled Release of Bioactive Materials, Edinburgh, UK, July, 2015.
118. Enhancing Macrophage Uptake of Rifampicin, 3rd International TB-Meeting, October, 2015 Parma, Italy

119. Development of Coenzyme Q10 Nano-emulsions for a Nebulization Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2015.
120. Formulation and Characterization of Dextromethorphan Thin Films, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2015.
121. Manufacture and Characterization of Rifampicin Particles for Aerosolization, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2015.
122. Polymeric Coating of Endotracheal Tubes for Local Drug Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2015.
123. Stability Characterization of Nano-Emulsions Intended as a Vehicle for Aerosol Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2015.
124. Preparation and Evaluation of Dextromethorphan Containing Thin Films, ExcipientFest 2015, Baltimore, MD, April, 2015.
125. Development of Coenzyme Q10 Nano-Emulsions for Nebulization Delivery, 43rd International Symposium on Controlled Release of Bioactive Materials, Seattle, WA, July, 2016.
126. Polyethylene Glycol Coating of Endotracheal Tubes for Local Delivery, 43rd International Symposium on Controlled Release of Bioactive Materials, Seattle, WA, July, 2016.
127. Manufacture and Assessment of a Novel 3D Printed Induction Port for Cascade Impactor Analysis, ExcipientFest 2017, Providence, RI, April, 2017.
128. Effect of Drug Concentration on Viscosity of Submicron Dispersions of Coenzyme Q10, ExcipientFest 2017, Providence, RI, April, 2017.
129. Investigating ACI Performance of a Salbutamol pMDI Formulation Using a Modified 3D Printed Induction Port, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2017.
130. Effect of Drug Concentration on surface tension and the rheology of Submicron Dispersions of CoenzymeQ10, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2017.
131. Reducing the Sol-Gel Transition of Hypromellose 2910 with Highly Electronegative Ion Containing Gelling Aids, ExcipientFest 2018, San Juan, PR, May, 2018.
132. Oral Gelling Liquid Formulations for Dental Remineralization, ExcipientWorld 2019, National Harbor, MD, May, 2019.
133. Preparation of Drug Containing Core Microparticles for use in Taste Masking Applications, 43th International Symposium on Controlled Release of Bioactive Materials, Las Vegas, NV, June, 2020.
134. Determining the design space of intermediate core microparticles obtained from spray dried acrylic polymers for taste masking bitter drugs, Annual Meeting of the American Association of Pharmaceutical Scientists, Virtual Meeting, October, 2020.
135. Enhanced Dissolution of a Poorly Soluble Drug Using a Spray Drying Technique, Annual Meeting of the American Association of Pharmaceutical Scientists, Philadelphia, PA, October, 2021.

136. The Effect of 3D Printed Mimetic Human Induction Ports on the Deposition of Inhalation Aerosols, UNM College of Pharmacy Annual Research Day, Albuquerque, NM, April, 2022.
137. Variability in 3D Print Weight for Novel Solid Oral Dosage Form Components, UNM College of Pharmacy Annual Research Day, Albuquerque, NM, April, 2022.
138. Modifying Drug Release from Microparticles Prepared by Spray Drying Using a 3-Fluid Nozzle, Annual Meeting of the American Association of Pharmaceutical Scientists, Boston, MA, October, 2022.
139. 3D Printed Mimetic Human Induction Ports Effects the Deposition of Inhalation Aerosols, American Society of Health-System Pharmacists (ASHP) Midyear Meeting, Las Vegas, NV, December, 2022.

XV. Book Contributions and Editorials

1. J.T. McConville, Preface for *Advanced Drug Formulation Design to Optimize Therapeutic Outcomes*, (Eds.) Robert O. Williams III, David R. Taft, J.T. McConville, Informa Healthcare, New York, NY, September, 2007.

2. J.T. McConville, N.P. Wiederhold, Invasive Pulmonary Aspergillosis: Therapeutic and Prophylactic Strategies, In *Advanced Drug Formulation Design to Optimize Therapeutic Outcomes*, (Eds.) Robert O. Williams III, David R. Taft, J.T. McConville, Informa Healthcare, New York, NY, September 2007.

3. J.T. McConville, F.J. McInnes, A.C. Ross, Preface for Innovative Inhalation Technologies: Special Edition, *Drug Development and Industrial Pharmacy*, 34(2008) 1-2.

4. S. Thitinan, J.T. McConville, Pulsatile Drug Delivery, In *Controlled Release: Oral Dosage Forms*, Eds. Patrick Crowley, Clive Wilson, Controlled Release Society Books, St. Paul, MN, 2011.

5. Y-Ju Son, J.T. McConville, In Vitro Performance Testing for Pulmonary Drug Delivery, In *Controlled Release Science and Technology: Pulmonary Delivery*, (Eds.) Hugh Smyth, Anthony Hickey, Controlled Release Society Books, St. Paul, MN, 2011.

6. J.O. Morales, A.B. Watts, J.T. McConville, Mechanical Particle Size Reduction Techniques, In *Formulating Poorly Water Soluble Drugs*, (Eds.) Dave Miller, Alan Watts, Robert O. Williams III, Springer Publishing Company, New York, NY, 2011.

7. J.O. Morales, J.T. McConville, Polymer Drug Delivery Systems for Sustained Mucoadhesion in the Respiratory Tract. In *Polymers for Pulmonary Drug Delivery*, (Eds.) H.D.C. Smyth, I. Saleem, J.T. McConville, iSmithers, Shrewsbury, UK, 2013.

8. P. Du, J.T. McConville, Regulatory Aspects of Pulmonary Delivery of Polymers. In *Polymers for Pulmonary Drug Delivery*, (Eds.) H.D.C. Smyth, I. Saleem, J.T. McConville, iSmithers, Shrewsbury, UK, 2013.

9. J.T. McConville, Polymer Drug Delivery Systems Targeting the Alveolar Macrophages. In *Polymers for Pulmonary Drug Delivery*, (Eds.) H.D.C. Smyth, I. Saleem, J.T. McConville, iSmithers, Shrewsbury, UK, 2013.

10. J.O. Morales, J.T. McConville, Preface for Buccal Drug Delivery Theme Issue, *Drug Development and Industrial Pharmacy*, 40(2014), 577–578.

11. J.T. McConville, Preface for Special Focus: Pharmaceutical Dosage Form Design Influence on Drug Pharmacokinetics, *Drug Development and Industrial Pharmacy*, 41(2015), 1921.

12. J.T. McConville, Preface for Special Focus: Transdermal, Topical and Folicular Drug Delivery Systems, 42(2016), 845.

13. J.T. McConville, Preface for Special Focus: Ocular and Ophthalmic Drug Delivery Systems, 42(2016), 513.

14. J.T. McConville, Preface for Special Focus: Current developments in oral drug administration, *Drug Development and Industrial Pharmacy*, 43 (2017), 699.

15. J.T. McConville, J.O. Morales, Preface for Selected abstracts from Excipient Fest 2017, *Drug Development and Industrial Pharmacy*, 44 (2018), 868.

16. J.T. McConville, R. Gala, J.O. Morales, Preface for Special Issue: Thin Film Technologies, *International Journal of Pharmaceutics*, November, 2019.

XVI. Invited Talks, Sessions, and Workshop Presentations

1. *Microwave Dielectric Analysis of Wet Granulations for Erodible HPMC Tablets*, Proceedings of the 138th British Pharmaceutical Conference, Glasgow, United Kingdom, September, 2001.

2. *Chronopharmaceutical Drug Delivery*, University of Texas at Austin, Austin, TX, October, 2001.

3. Workshop Presenter: *Particle Engineering Technologies: Theory and Practice*, Annual Meeting of the American Association of Pharmaceutical Scientists, Baltimore, MD, November, 2004.

4. *Capsule Filling and Topical Formulations*, Science Camp Presentation, Priscilla Pond Flawn Child and Family Laboratory, University of Texas at Austin, Austin, TX, June, 2005.

5. *Pre-Clinical Development Studies with Poorly Water-Soluble Drugs*, Universidade Federal de Minas Gerais, Belo Horizonte, Brasil, June, 2005.

6. *Targeted High Lung Concentrations of Itraconazole using Nebulized Dispersions in a Murine Model*, 1st Joint Symposium on the Future Prospects of Pharmaceutical Sciences, Hoshi University, Tokyo, Japan, October, 2005.

7. *Pre-Clinical Development Studies with Poorly Water-Soluble Drugs*, University of Louisiana at Monroe, Monroe, LA, January, 2006.

8. *The Effective Delivery of Itraconazole for the Treatment of Acute Fungal Infections*, University of Mississippi, Oxford, MS, January, 2006.

9. *Targeted High Lung Concentrations of Itraconazole using Nebulized Dispersions in a Murine Model*, University of Texas at Austin, Austin, TX, February, 2006.

10. *Enhanced Therapeutic Outcomes using Targeted Itraconazole Delivery in a Murine Model*, Long Island University, Brooklyn, NY, February, 2006.

11. *Targeted Treatment of Infectious Diseases to the Lung*, Virginia Commonwealth University, February, 2007.

12. *Targeted Lung Delivery of Antifungals: Preclinical Studies using Itraconazole Nanoparticles*, Respiratory Drug Delivery Europe 2007, Paris, France, April, 2007.

13. *Preclinical Studies with Poorly Water Soluble Drugs*, University of Strathclyde, Glasgow, UK, July, 2007.

14. *Antifungal Prophylaxis to Treat Pulmonary Aspergillosis*, GEA-NUS 10th Anniversary Celebration & Pharmaceutical Technology Seminar, Singapore, December, 2007.

15. *Novel In Vitro Dissolution Testing Methods for Inhalation Formulations*, Dissolution Testing, Bioequivalence & Bioavailability Strategies Meeting, London, United Kingdom, June 2008.

16. *Dissolution Testing of Inhalation Products*, Copley Scientific Ltd, London, United Kingdom, June 2008.

17. *Modification of the USP Type II Dissolution Testing Apparatus for Powder Formulations*, Novartis, Basel, Switzerland, July 2008.

18. *The Use of Renewable Ingredients for Pharmaceutical Formulations*, Tate & Lyle, Decatur, September 2008.

19. *Improved Therapy by Direct Lung Targeting for the Treatment of Pulmonary Aspergillosis*, Purdue University, September, 2008.

20. Attendee/Observer at the Aerosol Advisory Board Meeting, United States Pharmacopeia Headquarters, Rockville, MD, January, 2009.

21. *Formulation and Characterization of Prosolv® Fast Disintegrating Tablets*, Prosolv® Advisory Board Meeting, San Juan, Puerto Rico, April, 2009.

22. Workshop Presenter: Advances in the Development of Oral Controlled Release Pharmaceutical Forms and/or Site Specific Gastrointestinal Tract Delivery and Pulmonary Delivery Systems: *An Introduction to Pulmonary Drug Delivery*, Santiago, Chile, October, 2009.

23. *Formulation and Characterization of Fast Disintegrating Tablets Containing Renewable Ingredients*, 2nd Joint Symposium on the Future Prospects of Pharmaceutical Sciences, Hoshi University, Tokyo, Japan, October, 2009.

24. *Dissolution Testing of Aerosol Powder Formulations*, Novartis, Horsham, UK, December 2009.

25. Workshop Presenter: *An Introduction to Buccal Drug Delivery*, Advances in Pharmaceutical Technology and Pharmaceutical Engineering, Santiago, Chile, October, 2010.

26. *Fighting Dysphagia with Orally Disintegrating Tablets*, Functional Foods for Chronic Diseases: Science and Practice, Las Vegas, March, 2010.

27. *Formulation of Rapidly Disintegrating Tablets to Combat Dysphagia*, Prosolv® Advisory Board Meeting, Miami, FL, April, 2011.

28. Workshop Moderator and Presenter: *Developing Pharmaceutical Products for Controlled Pulmonary Delivery*, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington, DC, October, 2011.

29. Workshop Presenter and Panel Discussion Member: *Dissolution Testing to Meet Formulation Challenges*, 39th International Symposium on Controlled Release of Bioactive Materials, Quebec City, Canada, July, 2012.

30. Speaker and Panel Discussion Member: *A Prospective Dissolution Test Design: Controlling the Important Variables*, Respiratory Drug Delivery 2012, Phoenix, AZ, 2012.

31. Workshop Presenter and Panel Discussion Member: *Setting Release Specifications for in vitro Testing of Controlled Release Dosage Forms: Dissolution Testing to meet Formulation Challenges*, 39th International Symposium on Controlled Release of Bioactive Materials, Quebec City, Canada, July, 2012.

32. Visiting Professor and Workshop Presenter: *An Introduction to Pulmonary Drug Delivery*, Advances in Pharmaceutical Technology and Pharmaceutical Engineering, Santiago, Chile, April, 2013.

33. *Trans-Mucosal Buccal Drug Delivery,* New Mexico Society of Health-System Pharmacists (NMSHSP) Balloon Fiesta Symposium, Albuquerque, NM, October, 2013.

34. *Inhaled Therapeutics for Lung Cancer*, Drug Delivery to the Lungs Conference (DDL24), Edinburgh, UK, December, 2013.

35. *Development of a Single Capsule Multiple Dose Regimen*, (New Mexico Pharmacist Association (NMPhA) Mid-Winter Meeting, January, 2014.

36. Session Chair and Moderator: *Macromolecule Drug Delivery: Challenges and Triumphs*, AAPS National Biotechnology Conference, San Diego, CA, May, 2014.

37. *Use of Cationic Polymethacrylate Derivatives for Oral Mucosa Drug Delivery*, 1st International Society for Biomedical Polymers and Polymeric Biomaterials Conference, Washington DC, July, 2014.

38. *Enhancing Macrophage Uptake of Rifampicin,* 3rd International TB-Meeting: Inhaled Therapies for Tuberculosis and Other Infectious Diseases, October, 2015, Parma, Italy.

39. Session Chair and Moderator: *Challenges and Future Prospects of Alternative Delivery of Biologics*, American Association of Pharmaceutical Sciences Annual Meeting, Orlando, FL, October, 2015.

40. *Development of a Buoyant Gastroretentive Dosage Form*, University of Sarajevo, Sarajevo, Bosnia and Herzegovina, June, 2016.

41. *Cascade Impactor Performance using 3D Printed Induction Port Designs*, American Association of Pharmaceutical Scientists Rocky Mountain Discussion Group 5th Annual Meeting, Albuquerque, NM, October, 2017.

42. *Using Highly Electronegative Gelling Aids with Hypromellose 2910,* 4th World Congress & Expo on Pharmaceutics and Drug Delivery Systems, Milan, Italy, March, 2019.

43. *Cascade Impactor Performance using Anatomically Appropriate 3D Printed Induction Port Designs*, University of Cork, Cork, Ireland, August, 2019.

44. *Taking it Slow: Reduced Velocity Aerosols*, Inspire Me, San Francisco, CA, June, 2019.

45. *Oral Gelling Liquid Formulations*, Rainforest Innovations, Albuquerque, NM, August, 2021.

XVII. Intellectual Property

1. Enhanced Delivery of Drug Compositions to Treat Life Threatening Infections, United States Patent US9061027 B2 (WO2006026502A1), Issue date: Jun 23, 2015.

2. Enhanced Delivery of Immunosuppressive Drug Compositions for Pulmonary Delivery, United States Patent US9044391 B2, Issue Date: Jun 2, 2015.

3. Stabilized Hot Melt Extrusion Composition with Small Drug Particles, United States Patent US9504658 B2 (WO2007001451A9), Issue date: Nov 29, 2016.

4. Enhanced Delivery of Immunosuppressive Drug Compositions for Pulmonary Delivery, United States Patent US10231955 B2, Issue Date: Mar 19, 2019.

5. Treatment of Pulmonary Fungal Infection with Voriconazole via Inhalation, Non-Provisional Patent Application (PCT/US2009/043027), filed: May 6, 2009.

6. Bioadhesive Films for Local and/or Systemic Delivery: Non-Provisional Patent Application (PCT/US2013/032490 - WO 2014/065870), filed: March 15, 2013.

7. Wireless Dispensing Device Monitor: Provisional Application (US62/796,678), filed: Jan 25, 2019.

8. Coenzyme Q10 Aerosol: Non-Provisional Application (PCT/US2016/039173 - WO 2016/210226), filed: June 24, 2016.

9. Coenzyme Q10 Aerosol: National Application (15/738,512), filed Dec 20, 2017.

10. Drug-eluting medical devices coatings: Provisional Application (US62/948,469), filed: Dec 16, 2019.

11. Oral Gelling Liquid Formulations: Non-Provisional Application (US16/839,385), filed Feb 13, 2020.

12. Thermally Gelling Drug Formulations: Non-Provisional Application (US16/947,224), filed Jul 13, 2020.

EXHIBIT 13

UNREDACTED PUBLIC VERSION

Exhibit 13
Plaintiffs' Deposition Designations

Kocherlakota, Chandrashekar 7/31/2024	Objections	Counter Designations	Objections to Counter Designations
20:17-21			
21:4-13			
21:15-16			
22:4-16			
25:9-26:3			
27:7-28:3			
28:15- 20			
32:1- 9			
32:22-33:19			
33:22-34:3			
34:5			
35:24-36:1			
36:3- 37:10			
38:7-9			
38:11-14			
39:3-5			
39:8-14			
9:16-18			
40:5-6			
40:8-15		40:16-42:2	AT, D, I, IC, M, R, F, K, NE, S
42:9-11			
42:14-19			
43:5-6			
43:13-16			
44:1-5			
44:7-11			
45:6-8			
45:10-14			
45:16-20			
Singh, Ajeet 7/26/2024			
83:13-84:10			
84:14-16			
84:18-23			
85:2-10			
88:5-89:5			

89:15-17			
90:8-91:1			
	Objections	**Counter Designations**	**Objections to Counter Designations**
91:7-10			
117:9-23		112:18-114:23; 116:10-117:8; 122:6-132:10; 171:25-175:5; 177:25-178:18	I, IC, F, AT, AU, C, M, X, P, R, MD, NE,
118-10-120:14		112:18-114:23; 116:10-117:8; 122:6-132:10; 171:25-175:5; 177:25-178:18	I, IC, F, AT, AU, C, M, X, P, R, MD, NE,
120:16-17		112:18-114:23; 116:10-117:8; 122:6-132:10; 171:25-175:5; 177:25-178:18	I, IC, F, AT, AU, C, M, X, P, R, MD, NE,
152:19-153:8			
156:14 -157:2			
158:7-15			
161:22-162:12			
Nair, Sabita 7/24/2024			
6:6-7:21			
8:11-19			
9:14-10:5			
10:18-20			
10:24-11:1			
11:19-12:1			
12:5-8			
16:15-22			
20:17-24			
21:4-16			
23:2-5			
23:21-24:22			
24:24-25			
25:6-18			
26:3-10			
26:23-27:7			
27:12-28:17			
29:2-15			
29:19-20			

29:22-24			
30:13-22			
30:24-31:12			
33:16-25		34:7-12	C, F, H, I, IC, K, M, R, S, SC
34:21-25			
35:2-13			
35:15-23			
37:11-38:14		38:15-40:8	F, M, R, SC, C, F, I, IC, K,
40:9-25			
41:4-10			
43:3-6			
	Objections	**Counter Designations**	**Objections to Counter Designations**
47:15-22			
48:5-11			
48:20-49:4			
50:5-18			
50:21-51:	Incomplete		
52:17-18			
54:16-55:11			
55:22-57:1	Scope		
59:17-60:20	Scope		
61:1-14	Scope		
61:17-21	Scope		
63:14-19			
63:23-64:3			
64:5-6		64:7-11	S, F, I, IC, SC, K,
64:12-23			
67:20-68:19			
68:20-22			
69:23-25			
70:8-13			
71:19-72:6			
72:16-19			
72:21-73:4			
73:13-74:1			
74:6-75:14			
75:19-23			
75:25-76:17			
76:19-25			
78:19-21			
81:16-82:2			

84:4-7			
84:17-21			
85:12-13			
87:2-5			
87:22-88:1			
88:9-19			
94:9-13			
81:16-82:2			
84:4-7			
84:17-21			
85:12-13			
87:2-5			
87:22-88:1			
	Objections	**Counter Designations**	**Objections to Counter Designations**
88:9-19			
94:9-13			
95:4-15			
95:21-22			
95:25-96:1			
97:25-99:19			
99:20-100:11			
100:13-102:7			
102:9-105:2			
106:6-107:4			
107:9-12			
107:14-108:18			
108:23-109:1			
109:14-110:5			
111:6-7			
111:12-14			
Nagaraju, Banda 7/23/2024			
16:13–17:9			
17:22-18:3			
18:4-18:13			
18:14-19:3			
19:8-20:19			
22:2-22:10			
22:11-23:8			
23:10-24:2			
24:3-24:21			

24:22-25:22			
25:24-26:5			
28:19-30:9			
31:22-32:23			
36:19-37:9			
40:16-44:11			
45:17-47:22			
48:10-12			
53:21-54:4			
56:18-57:2			
59:22-60:1			
69:6-21			
73:5-8			
75:18-21			
Karnik, Kuldeep 7/17/2024			
11:18-17:15			
17:16-25:13			
25:14-31:3			
31:24-35:2			
35:5-38:17			
38:18-46:19			
46:20-57:24			
61:21-68:7			
68:10-80:19			
81:11-94:1			
94:2-106:21			
107:13-109:16			
109:19-123:8			
123:9-133:21			
135:9-136:19			
136:20-140:2			
149:12-150:23			
152:7-153:9			

PLAINTIFF'S OBJECTIONS KEY

Code	Objection
A	Argumentative
AT	Attorney objections not removed
AU	Authenticity or Identification (FRE 901)
B	Violates Best Evidence Rule (FRE 1002-1004)
C	Compound
D	Duplicative/Cumulative
F	Lack of Foundation (FRE 602)
H	Hearsay/Improper Use of Deposition (FRE 801-802: FRCP 32)
I	Improper/Incomplete Designation (FRE 106: FRCP 32(a)(6))
IC	Improper Counter-Designation (FRE 106: FRCP 32(a)(6))
ID	Improper Designation of a Witness To Be Called Live (FRCP 32)
IO	Improper Lay or Expert Opinion (FRE 701-703)
K	Lack of Personal Knowledge/Incompetent (FRE 602)
LC	Improper Legal Conclusion (FRE 403)
M	Misleading/Mischaracterizes Prior Testimony
MD	Mischaracterizes Underlying Document (FRE 401-403)
NE	Assumes Facts Not In Evidence (FRE 103)
NR	Nonresponsive
P	Prejudice/Confusion/Delay/Waste of Time (FRE 403)
R	Relevance (FRE 401/402)
S	Calls for Speculation (FRE 602)
SC	Beyond the Scope of the Witness's Testimony as a Corporate Representative
U	Improper Use Against Other Parties or For Other Purposes (FRE 105)
V	Vague/Ambiguous/Overbroad
X	Incomplete Document (FRE 106)
Y	Wrong Document or Incorrectly Described
Z	Reserved Because Exhibit Has Not Been Provided, the Copy Provided is Illegible, and/or the Entry Includes Multiple Documents

EXHIBIT 14

UNREDACTED PUBLIC VERSION

EXHIBIT 14

ACCORD'S DEPOSITION DESIGNATIONS

Singh, Ajeet 7/26/2024

Accord Designations	Objections	Counters	Objections to Counters
8:17-20			
14:8-15:21			
16:23-17:3	I,		
100:4-102:3	I, AT		
103:7-105:24	I	105:25 – 106:18	
106:19-107:6		142:18-22; 143:2-144:6; 144:18-145:9	
108:4-7			
112:19-114:23	I		
116:10-117:8	I, M	120:18-121:9	
122:6-132:10	I, D, K, AT, M, LC, F, NE	132:11-133:17; 165:11-14; 169:4-14; 170:13-171:2; 169:18-22;	
146:16-147:18	AT, I,		
161:22-162:12			
166:10-168:16	M, C, D, F, K, MD, R, S,		
171:25-175:5	C, I, , M, F, K		
177:25-178:18	AT, I,	171:25-172:8; 178:19-179:18; 179:24-181:11	

Chandrashekar, Kocherlakota 7/31/2024

Accord Designations	Objections	Counters	Objections to Counters
6:6-9			
8:19-23			
28:9-10			
28:21-30:6	NE, R, V,AT		
30:20-31:6	NE, R, V, AT		
32:5-9			
33:25-35:9	NE, R, M, V, D, AT		
37:11-19	F, V, AT		
38:2-14			

Accord Designations	Objections	Counters	Objections to Counters
38:22-41:18	F, NE, R, V. D, AT		
43:5-46:19			
46:22-47:23	I, IC, V, M		
48:5-52:6	I, V, S, R, NE, M, AT		
53:16-54:4	D, V, AT		
54:21-57:2	D, V, F, NE, R, AT		
57:10-60:8	V, R, F, NE, M, D, AT	57:3-9	
69:3-70:25	IO, LC, V, AT		
72:2-16	I, AT, V, MD,		
73:1-21	D, M, AT		
74:11-76:5	V, M, D, AT		
76:13-19	V, M, D, AT		
78:21-81:3	V, M, D, AT		
81:7-16	I, V, M, AT		
82:2-15	V, AT	82:16-21	
84:23-25	I, IC, V,		
85:2-87:23	V, C, M, D, I, , AT		
88:9-89:9	V, R, NE, AT,	89:10-12	
97:13-16	I, IC, V		
98:10-99:13	V, AT, M,	99:14-19	
107:4-110:9	D, V, AT, M		

Nagaraju, Banda 7/23/2024

Accord Designations	Objections	Counters	Objections to Counters
5:20-21			
11:12-14			
11:21-24	I,		
12:23-24			
13:10-14			
22:11-21			
23:10-16			
28:19-29:20			
30:11-24	D, AT, V, I,	30:21-31:7	
31:1-32:8	I, , V,	32:10-23	
32:18-33:4			
33:11-34:21	V, M, D, AT	22:6-10	
45:6-47:21			
56:2-3	I,		
56:25-58:7			

Accord Designations	Objections	Counters	Objections to Counters
59:10-60:12			
64:20-65:5		59:22-60:6	
65:23-66:19		59:22-60:6	
67:3-68:3			
68:11-18			
69:6-7			
69:17-21			
70:21-72:9		69:22-70:19	
72:11-12			
73:2-75:4		75:6-17	
75:18-76:12	V, D, M, AT		
76:14-23	V, D, M,		

EXHIBIT 15

UNREDACTED PUBLIC VERSION

Exhibit 15

Brief Statement of Intended Proofs [D. Del. LR 16.3(c)(8)-(10)]

1. Plaintiffs bear the burden to prove that Accord's Abbreviated New Drug Application (ANDA) products infringe the asserted claims of the '952 Patent. Plaintiffs intend to show that Accord's ANDA products infringe the asserted claims.

2. Plaintiffs bear the burden to prove that Accord will induce infringement or contribute to the infringement of the asserted claims of the '952 Patent. Plaintiffs intend to show that Accord will infringe the asserted claims.

3. Accord bears the burden of proof on their various assertions of invalidity (*i.e.,* obviousness, non-enablement, indefiniteness, and lack of written description) of the asserted claims of the '952 Patent.

4. Accord also bears the burden of proof that the asserted prior art references are actually prior art to the '952 Patent.

5. This case does not involve a claim for damages.

6. Plaintiffs request the following relief from the court:

a) A judgment that claims 1–4 of the '952 Patent are not invalid, are enforceable, and are infringed by Accord's ANDA Products, and that Accord's making, using, offering to sell, or selling in the United States, or importing into the United States of Accord's ANDA Products, will infringe those claims of the '952 Patent.

b) An order that the effective date of any approval of Accord's ANDAs be not earlier than the expiration date of the '952 Patent, including any extensions and/or additional periods of exclusivity to which Novartis is or becomes

entitled.

c) A permanent injunction restraining and enjoining Accord's their affiliates, their subsidiaries, and their officers, agents, attorneys, and employees, and those acting in privity or concert therewith, from engaging in the commercial manufacture, use, offer for sale, sale and/or import of Accord's ANDA Products until the expiration of the '952 Patent, including any extensions and/or additional periods of exclusivity to which Plaintiffs are or become entitled to;

d) An order dismissing Accord's counterclaims with prejudice;

e) An order declaring this case exceptional under 35 U.S.C. § 285 and granting Plaintiffs its attorneys' fees;

f) An order awarding Plaintiffs its costs and expenses; and

g) An order granting such other and further relief as this Court may deem just and proper.

EXHIBIT 16

ACCORD'S BRIEF STATEMENT OF INTENDED PROOFS

UNREDACTED PUBLIC VERSION

ACCORD'S BRIEF STATEMENT OF INTENDED PROOFS

1. Accord will prove that the asserted claims of U.S. Patent No. 10,993,952 are invalid for indefiniteness, because the scope of "about 70% to about 75% ethanol" (claim 1) and "about 70% ethanol" (claim 4) are not reasonably certain to a POSA. Specifically, a POSA cannot know with reasonably certainy what the outer bounds of the claim are or how to make such a determination.

2. Ingenus will not be able to prove that Accord's ANDA product infringes any claim of the 952 patent, specifically that Accord's ANDA product contains "an ethanol content of about 70% to about 70% 75%" (claim 1) "cyclophosphamide in a concentration of about 23%" and "an ethanol content of about 70%" (claim 4). Accord's ANDA product contains 68.74% ethanol and 22.17% cyclophosphamide.

3. Ingenus will not be able to resort to infringement under the doctrine of equivalents because (1) DOE is not available to further expand the scope of "about" claims; (2) the doctrines of prosecution history estoppel and the disclosure-dedicaiton rule bar resort to equivalents. Specifically, the specification discloses broader ranges, but the applicants surrendered such scope for reasons related to patentability.

4. Accord will prove that the asserted claims of the 952 patent are invalid for obviousness.

5. Accord will prove that the prior art taught forming stable liquid cyclophosphamide formulations using organic solvents, primarily ethanol, with smaller amounts of polyethylene glycol and propylene glycol. Accord will prove that it would have been obvious to a POSA to arrive at the claimed invention using routine experimentation optimizing the prior art teachings. Accord will further prove that there is nothing critical about the claimed ranges.

6. Accord will prove that there is no objective evidence demonstrating non-obviousness.

7. For example, Accord will prove that the Examiner erred in finding unexpected results, as at best the claimed formulations exhibit a modest increase in stability over specific formulations of Alam and Palepu. Accord will show that this comparison does not show unexpected results (especially in kind) and that it is not an accurate comparison as it does not include the full teachings of Palepu and Alam, let alone address the teachings of other prior art references such as Shaik and Tait. For example, the testing shown in Shaik shows fewer total impurities under the same conditions than the claimed formulations.

8. Accord will show that Ingenus cannot demonstrate a longfelt but unmet need demonstrating non-obviousness. Specifically, the need was already moderated by the availability of lyophilized formulations, and was met by the prior art including Palepu and Shaik.

9. Accord will show that its use of a similar formulation as Ingenus was made for economic reasons and does not indicate non-obviousness.

10. Accord will prove that the asserted claims are invalid as failing to meet the written description and enablement requirements of 35 U.S.C. § 112.

11. Accord will prove that the specification fails to either describe or enable the full scope of the asserted claims because it provides stability data for only a single formulation even arguably falling within the scope of the claims and did not possess stable formulations for the full scope of the claims.